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Does nicotine help fight COVID-19? The science behind a novel hypothesis

Researchers in France have put forward a hypothesis that the presence of nicotine actually equips the body to fight COVID-19.

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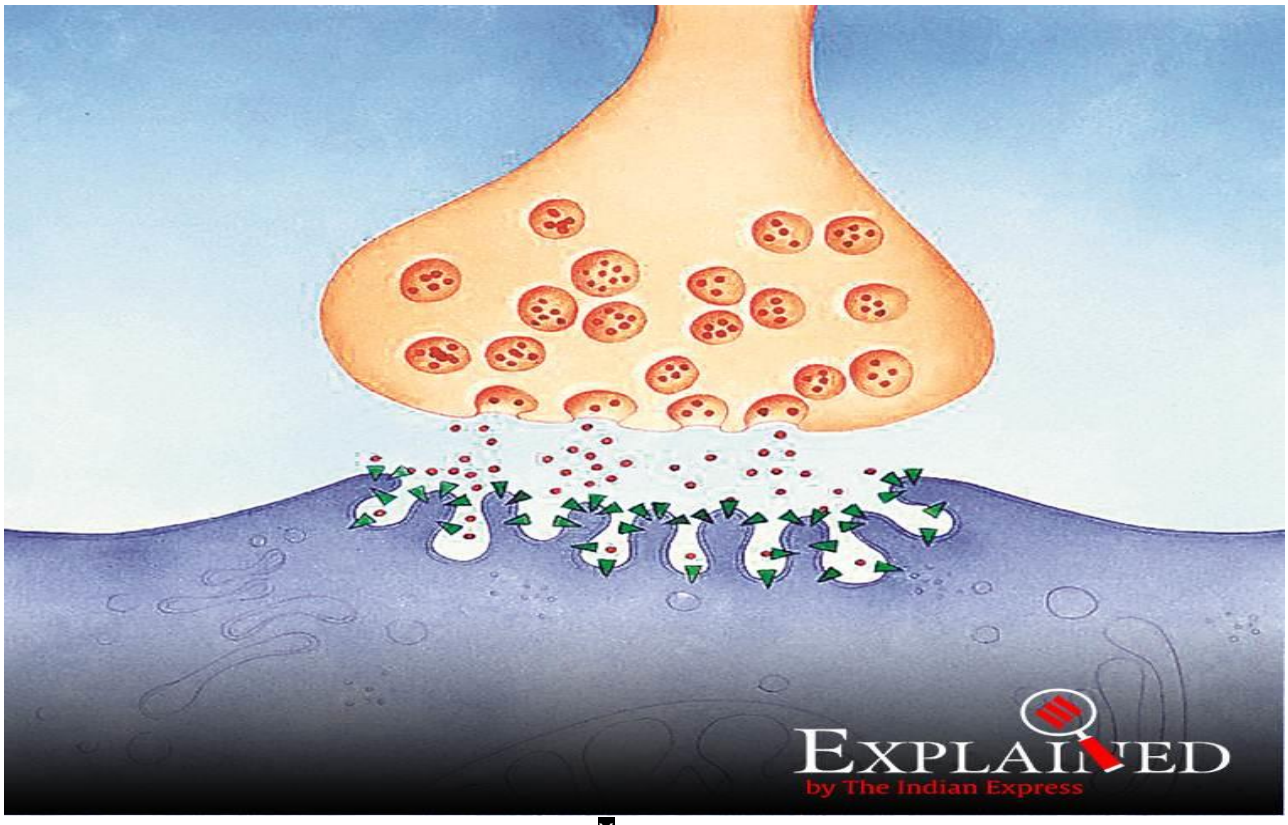

Schematic diagram shows nicotine (or acetylcholine) binding to receptors in the cell (triangles). These receptors are at the centre of the hyopthesis that the presence of nicotine helps resist the coronavirus SARS-CoV2. (Source: Institut Pasteur)

Smoking kills. So does COVID-19, and if a smoker contracts the disease, conventional wisdom should suggest that he or she faces a higher risk of severe illness or death.

Now, researchers in France have turned that conventional wisdom on its head. They have put forward a hypothesis that the presence of nicotine actually equips the body to fight COVID-19. And they are conducting trials to test the hypothesis.

What is the basis of the hypothesis?

It has been postulated by researchers from a number of leading French institutions — the government research institutes CNRS and Inserm, the hospital network Assistance Publique-Hôpitaux de Paris, Sorbonne University, Collège de France, and Institut Pasteur. They have described the hypothesis in a paper written for the journal Comptes Rendus de Biologie de l'Académie des sciences, and published a version on a pre-print server.

"The researchers' hypothesis is based on the combination of two different but complementary scientific approaches," Institut Pasteur said in a statement. One of

these two approaches is based on a statistical analysis of COVID-19 deaths in a French hospital, and the other on the biochemistry of the human body.

What is the statistics-based approach?

It draws from an observation of the proportion of smokers among patients who died of COVID-19. These were patients at Pitié Salpétrière University Hospital, Paris. “In the hospitalised in-patients vs less severe out-patients, a smoking rate of 4.4% vs 5.3% was found, both very low against 25.4% in the general population. This finding has been confirmed by an independent study,” neuroscientist Jean-Pierre Changeux of Institut Pasteur said in an interview published by the European research initiative Human Brain Project.

The statistical study was led by Prof Zahir Amoura of the same hospital, together with Changeux. The two are among the authors of the study that describes the nicotine hypothesis. Changeux is also a pioneer in the study of a key chemical structure in the body, one that forms the basis of the second part of the hypothesis.

What is this chemical structure?

It is a kind of “receptor”. In the conversation around COVID-19, we have been hearing a lot about receptors. These are structures composed of protein, and they receive signals that may be integrated into the body. These signals can come from various substances, such as a hormone, a drug, or an antigen. For example, the surface of the human cell has receptors called ACE2, which open the door for the novel coronavirus SARS-CoV2 to enter the body.

At the centre of the nicotine hypothesis is a receptor that responds to nicotine as well as a chemical called acetylcholine. Hence its name: “nicotinic acetylcholine receptor”, abbreviated as nAChR. It is found in parts of the nervous system, muscle and certain tissues of organisms including humans. Changeux has researched this receptor for decades, with one paper dating back to 1965.

The widely accepted view is that the lungs of smokers are already compromised to various extents, hence they are likely to be more vulnerable to a disease that attacks the respiratory system. (Photo: Getty Images/Thinkstock)

How does this receptor fit into the hypothesis about nicotine?

Since nicotine is known to bind with the nAChR receptor, the second part of the hypothesis goes like this: If nicotine is present on the receptor, and the novel coronavirus arrives, then the nicotine would block the interaction.

In existing scientific knowledge, there is a possible pointer. The rabies virus is known to bind with the same receptor, and this interaction is driven by a sequence of genetic material that exists in the envelope around the rabies virus. “Amazingly there is a rather similar sequence in the envelope of SARS-CoV2. Its role is presently under investigation,” Changeux said in the interview.

And how will the researchers test their hypothesis?

Clinical studies are in progress, Institut Pasteur said. A Reuters report described the nature of the trial. It will involve groups of healthcare workers and patients wearing nicotine patches, and other groups wearing placebo patches. There will be 1,500 healthcare professionals in the trial, which will seek to assess whether those wearing the nicotine patches are more resistant to COVID-19 than those wearing the placebo patches.

How does this hypothesis sit against conventional views about smoking?

The widely accepted view is that the lungs of smokers are already compromised to various extents, hence they are likely to be more vulnerable to a disease that attacks the respiratory system. Some researchers have suggested, in fact, that the lower mortality rate among women patients of COVID-19 is a fallout of the fact that men tend to smoke more.

Again, the nicotine hypothesis involves the nAChR receptor, when SARS-CoV2’s main interactions are with a different receptor: ACE2. A study last month, in fact, looked at the expression of ACE2 among smokers and non-smokers. People who have smoked showed a 25% increase in ACE2 expression as compared to non-smokers, researchers reported in the American Journal of Respiratory and Critical Care Medicine. They suggested that smoking increases entry points for the novel coronavirus.

The Indian Express sent a mail to Changeux asking, among various questions, how far the cohort of COVID-19 patients in the statistical analysis of deaths was representative of the general population. He was yet to respond at the time of filing.

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