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Drug discovery and development

Researchers show how MRI data can help predict drug efficacy

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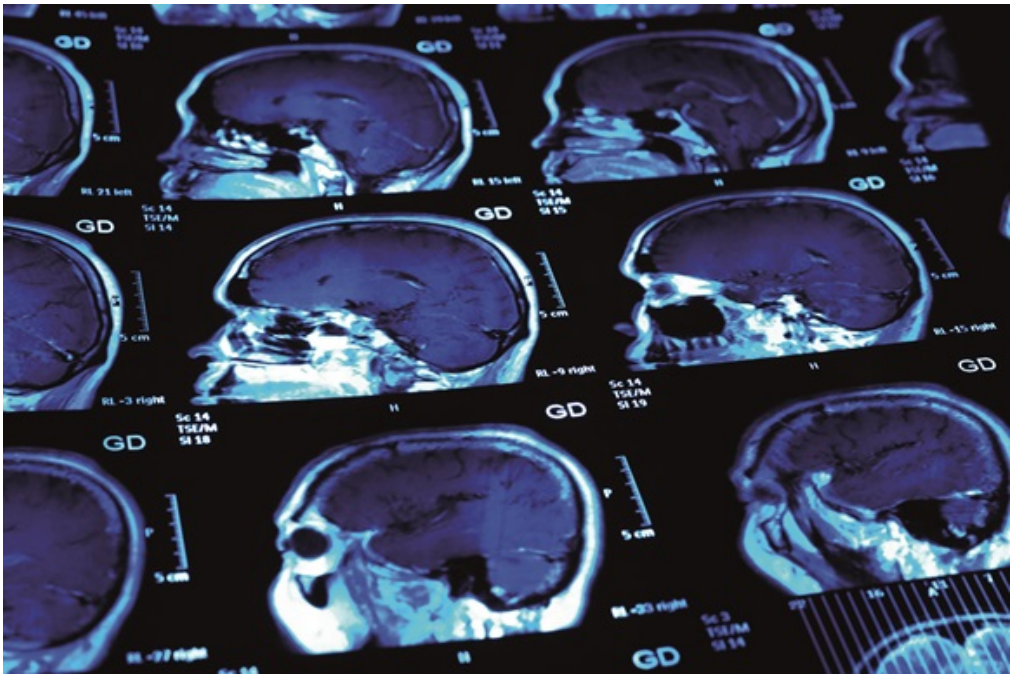
Data from brain scans allowed researchers to compare the effects of analgesic compounds on responses to pain.



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Scientists used data from functional magnetic resonance imaging to compare the effects of compounds on brain responses

Scientists have developed a method for using data from functional magnetic resonance imaging (fMRI) to shed light on how central nervous system (CNS) drugs cause changes in brain activity and to help predict drug efficacy, according to research published in *Science Translational Medicine*[1] on 11 February 2015.

The research team, led by investigators from the University of Oxford, analysed eight studies of six different analgesic compounds. Using fMRI data from these studies they were able to compare the effects of the compounds on brain responses relating to pain, enabling them to determine which brain responses were caused by the drug as opposed to placebos. Through this process, the investigators identified signatures of brain activity that were related to the efficacy of each compound.

“We were interested not so much in mapping specific areas of the brain, but in making a single inference from the data set, using all the data we have from the activity across the entire brain to determine whether analgesic compounds are present,” says Eugene Duff, a post-doctoral research associate at the Oxford Centre for Functional MRI of the Brain at the Nuffield Department of Clinical Neurosciences at John Radcliffe Hospital.

The new protocol could address some of the key problems facing those working on CNS drug discovery: namely, the expense and protracted time period for assessing the therapeutic potential of CNS drugs in initial human drug trials, in which the researchers note that efficacy can be both unreliable and hard to measure.

By using machine-learning techniques — an approach that produces algorithms from large fMRI data sets in order to learn which parts of the brain give an indication of whether an analgesic is present — the researchers were able to identify biological markers showing which drugs most consistently activated pain-sensitive regions of the brain, and contrast them with placebos. The biomarkers could be used in the future to evaluate new drug candidates for brain disorders that activate the same areas in the brain as existing drugs, says Duff, who notes that there have been few new pain medications developed in the past 10 to 20 years.

Given the high failure rate in clinical trials, he adds, the new approach would “potentially enable us to do smaller studies in the human population before devoting all these resources to more promising trials”.

In addition to its potential for improving the development of treatments for pain relief, the protocol could also be applied to other CNS conditions, including schizophrenia and obesity, the researchers say. One potential complication of extrapolating the process to such conditions, however, is the fact that they often involve a broader range of symptoms, making it more difficult to combine studies. Duff says the research team has recently adapted the protocol to include resting-state imagery to address this challenge. The approach could also be applied to personalised medicine in the future, Duff adds, by conducting studies of new patients to get an idea of how they respond to compounds and using machine learning to predict those responses as accurately as possible from an initial scan.

In a column accompanying the article[2], researchers Tor D Wager and Choong-Wan Woo of the University of Colorado note that the tests developed by Duff’s team could help researchers make difficult decisions about whether or not to continue clinical trials of new drugs that might be more likely to fail in more expensive phase IIb and phase III trials.

References:

[1]Duff EP, Vennart W, Wise RG *et al*. Learning to identify CNS drug action and efficacy using multistudy fMRI data. *Science Translational Medicine* 2015. doi/10.1126/scitranslmed.3008438.

[2]Wager TD & Woo C-W. fMRI in analgesic drug discovery. *Science Translational Medicine* 2015. doi/10.1126/scitranslmed3010342.

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