Thanks for the Memory

Experiments have backed what was once a scientific 'heresy', says Lionel Milgrom

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A bout homeopathy, Professor Madeleine Ennis of Queen's University Belfast is, like most scientists, deeply skeptical. That a medicinal compound diluted out of existence should still exert a therapeutic effect is an affront to conventional biochemistry and pharmacology, based as they are on direct and palpable molecular events. The same goes for a possible explanation of how homoeopathy works: that water somehow retains a "memory" of things once dissolved in it.

After many experiments, in 1988 Benveniste managed to get an account of his work published in Nature, speculating that the water used in the experiments must have retained a "memory" of the original dissolved aIgE. Homoeopaths rejoiced, convinced that here at last was the hard evidence they needed to make homoeopathy scientifically respectable. Celebration was short-lived. Spearheaded by a Nature team that famously included a magician (who could find no fault with Benveniste's methods - only his results), Benveniste was pilloried by the scientific establishment.

A British attempt (by scientists at London's University College, published in Nature in 1993) to reproduce Benveniste's findings failed. Benveniste has been striving ever since to get other independent laboratories to repeat his work, claiming that negative findings like those of the British team were the result of misunderstandings of his experimental protocols. Enter Professor Ennis and the pan-European research effort.

A consortium of four independent research laboratories in France, Italy, Belgium, and Holland, led by Professor M Roberfroid at Belgium's Catholic University of Louvain in Brussels, used a refinement of Benveniste's original experiment that examined another aspect of basophil activation. The team knew that activation of basophil degranulation by aIgE leads to powerful mediators being released, including large amounts of histamine, which sets up a negative feedback cycle that curbs its own release. So the experiment the pan-European team planned involved comparing inhibition of basophil aIgE-induced degranulation with "ghost" dilutions of histamine against control solutions of pure water.

In order to make sure no bias was introduced into the experiment by the scientists from the four laboratories involved, they were all "blinded" to the contents of their test solutions. In other words, they did not know whether the solutions they were adding to the basophil-aIgE reaction contained ghost amounts of histamine or just pure water. But that's not all. The ghost histamine solutions and the controls were prepared in three different laboratories that had nothing further to do with the trial.

The whole experiment was coordinated by an independent researcher who coded all the solutions and collated the data, but was not involved in any of the testing or analysis of the data from the experiment. Not much room, therefore, for fraud or wishful thinking. So the results when they came were a complete surprise.

Three of the four labs involved in the trial reported a statistically significant inhibition of the basophil degranulation reaction by the ghost histamine solutions compared with the controls. The fourth lab gave a result that was almost significant, so the total result over all four labs was positive for the ghost histamine solutions.

Still, Professor Ennis was not satisfied. "In this particular trial, we stained the basophils with a dye and then hand-counted those left coloured after the histamine- inhibition reaction. You could argue that human error might enter at this stage." So she used a previously developed counting protocol that could be entirely automated. This involved tagging activated basophils with a monoclonal antibody that could be observed via fluorescence and measured by machine.

The result, shortly to be published in Inflammation Research, was the same: histamine solutions, both at pharmacological concentrations and diluted out of existence, lead to statistically significant inhibition of basophile activation by aIgE, confirming previous work in this area.

"Despite my reservations against the science of homoeopathy," says Ennis, "the results compel me to suspend my disbelief and to start searching for a rational explanation for our findings." She is at pains to point out that the pan-European team have not reproduced Benveniste's findings nor attempted to do so.

Jacques Benveniste is unimpressed. "They've arrived at precisely where we started 12 years ago!" he says. Benveniste believes he already knows what constitutes the water-memory effect and claims to be able to record and transmit the "signals" of biochemical substances around the world via the internet. These, he claims, cause changes in biological tissues as if the substance was actually present.

The consequences for science if Benveniste and Ennis are right could be earth shattering, requiring a complete re-evaluation of how we understand the workings of chemistry, biochemistry, and pharmacology.

One thing however seems certain. Either Benveniste will now be brought in from the cold, or Professor Ennis and the rest of the scientists involved in the pan-European experiment could be joining him there.

This last notion, famously promoted by French biologist Dr Jacques Benveniste, cost him his laboratories, his funding, and ultimately his international scientific credibility. However, it did not deter Professor Ennis who, being a scientist, was not afraid to try to prove Benveniste wrong. So, more than a decade after Benveniste's excommunication from the scientific mainstream, she jumped at the chance to join a large pan-European research team, hoping finally to lay the Benveniste "heresy" to rest. But she was in for a shock: for the team's latest results controversially now suggest that Benveniste might have been right all along.

Back in 1985, Benveniste began experimenting with human white blood cells involved in allergic reactions, called basophils. These possess tiny granules containing substances such as histamine, partly responsible for the allergic response. The granules can be stained with a special dye, but they can be decolourised (degranulated) by a substance called anti-immunoglobulin E or aIgE. That much is standard science. What Benveniste claimed so controversially was that he continued to observe basophil degranulation even when the aIgE had been diluted out of existence, but only as long as each dilution step, as with the preparation of homoeopathic remedies, was accompanied by strong agitation.