Scientist deconstructs Séralini's PLOS GMO study: 'Failed attempt at redemption'

Gilles-Éric Séralini, a molecular biologist at the University of Caen in France, is hoping for redemption with a new paper about the effect of pesticides and genetically modified (GMO) feed on rats and mice. He hasn't earned that redemption.

A few years ago, Séralini suffered the ultimate humiliation for a scientist. The *Journal Food and Chemical Toxicology* retracted his high-profile study. The editors reviewed the raw data and found the results were "inconclusive" and did not back the conclusions that were loudly trumpeted in media headlines. The authors themselves eventually conceded that the study had serious flaws, noting in a press release that "the data are inconclusive, due to the rat strain and the number of animals used."

Other long-term studies, which were publicly funded, had uncovered no health issues with GMO corn or the herbicide glyphosate. The Japanese Department of Environmental Health and Toxicology released a 52-week feeding study of GM soybeans in 2007, finding "no apparent adverse effect in rats." In 2012, a team of scientists at the University of Nottingham School of Biosciences released a review of 12 long-term studies (up to two years) and 12 multi-generational studies (up to 5 generations) of GM foods in the same journal that published the Séralini paper, concluding there is no evidence of health hazards." Consequently, there was growing pressure on the journal to retract the original study since publication in 2012, along with other criticisms and an exchange of letters in the journal.

Now, Séralini has a new study, released July 2 after being delayed more than two weeks, in which the authors measured the levels of various pesticides, industrial chemicals and genetically engineered crops in 13 brands of laboratory rodent feed. (NOTE: An earlier version of the embargoed journal article had been distributed to journalists and numerous news outlets, and Séralini's own vanity site has broken the embargo.) There seems to be nothing wrong with the data itself. The results themselves of are not surprising given the currently planted genetically engineered crops and current pesticides usage.

- GLP has assessments from the latest Séralini study by scientists from around the world here.
- GLP has a profile of Séralini and his research here.

The authors take these unsurprising results and call into question the validity of everyone else's studies. The conclusion, as explained in a university press release, is unfounded: "It therefore appears that the cause of diseases and disorders found in laboratory rats has been too quickly attributed to the genetic characteristics of the species used." In other words, the rats are dying from GMOs and pesticides like glyphosate in feeds.

As a neuroscientist who works regularly with lab animals, I find these claims baffling.

These results do not mean much, given the absence of any data suggesting a correlation between diet and phenotype, a trait, in laboratory rodents. They have presented zero evidence from their own work or published work that feed contamination is an issue for laboratory animal health. They present no data on animal health and no data about which feeds, fed to which strains produce which pathological

phenotypes. They also completely ignore the fact that different strains of rodents have different phenotypes and rates of spontaneous pathology. The authors have made a huge logical leap in concluding that this data calls into question all historical data used as external controls.

Fortunately, the very historical data that the authors are attempting to discredit are unlikely to support their conclusion.

I would also argue that if such changes in the phenotype of well-characterized strains of lab rodents were occurring, the scientists who work with these animals would notice. When your control animals don't behave as expected (in their behavioral response, pathology, life span, reproductive success, anything really), this is a big red flag. If there was an issue with feed causing significant pathology in laboratory rodents, this is something that would be seen in labs around the world.

If we wanted to mine the existing data to address some of these concerns, here are a few question we can ask to explore if these chemicals or genetically engineered crops in laboratory feed affect the phenotype of laboratory rodents.

When genetically engineered crops were introduced in the 1990s, did control mice start having different phenotypes? We can pull the rates of spontaneous pathological effects from papers published before and after the introduction of the relevant genetically engineered crops and compare them. If there is no difference in control animals before and after the introduction of genetically engineered crops, then the GMO composition of laboratory feed has had no effect on the health of lab animals.

A study published last year by University of California-Davis animal geneticist Alison Van Eenennaam did just that with livestock. Her team examined almost 30-years of livestock studies, more than 100 billion animals, comparing their health before and after GMO feed became the norm. She found no difference in the animals.

1) Some commonly used lab strains have been used for 70+ years. The pesticide residues found in laboratory feed reflect the pesticides in current use, just as pesticide residues on food reflect current pesticide use. So an obvious question is: have the phenotypes of these mice changed as our pesticide use has changed?

When organochlorines were banned in the 1970s and replaced by organophosphates, was there a concurrent change in the phenotype of lab animals? As use of organophosphates has declined more recently, have we seen a change in the animals? As glyphosate has replaced more toxic herbicides have we seen a change in lab animal health? Again, we can assess this by comparing control animals in different decades. If the phenotype of control animals has been consistent, these changes in pesticides residues found in laboratory feed have had no effect on their health outcomes.

2) In the paper, the two feeds used in Italy had the highest amount of contaminants, according to the authors. This leads to the question: do lab animals in Italian labs have a different set of phenotypes as a result of eating this specific brand of feed? A more general way to put that question is to ask if the same lab strains fed feed with different contaminant profiles have different phenotypes?

We can easily mine existing data to address these questions. Let's look at Sprague-Dawley rats as an example to answer the first two questions. These rats were originally bred in 1925 so they have been used experimentally for enough time to answer questions 1 and 2 above. If we look at historical and current data on these animals, we can see if there have been any changes in their background phenotype. This has already been addressed in a rebuttal letter to a previous paper from Séralini's group. The rate does not appear to have changed.

> This specific breed of rats is well known to be prone to develop cancer with age and especially when there is no dietary restriction. For example, Prejean et al. (1973) noted a spontaneous tumour incidence of 45% in 360 Sprague–Dawley rats (179 males and 181 females) in an 18-month series of carcinogenesis experiments. The percentage of female rats with tumours was almost double that of males. Durbin et al. (1966) reported a mean incidence of 71%, the peak incidence in normally aging rats were age-related with abrupt increases in the rate of development of mammary tumour, one occurring at about the 500th and the other at about the 660th day of life, with the median age at 671 ± 41 days. Harlan, the company that marketed the animals, describes the high incidence of 76% of mammary gland tumours (predominantly fibroademonas) in females on Life-span and Spontaneous Disease of Sprague-Dawley. Keenan et al. (1995) describes spontaneous tumours in up to 87% of females and up to 71% of males fed ad lib. Dietary restriction significantly reduced the incidence of tumours.

3) To address the third question, we can compare data on control animals from studies done in different countries. Of course, the proper way to address these issues is to do a thorough meta-analysis of all control animals in studies, separated by strain. However, quick reviews of the literature for the incidence of spontaneous pathology doesn't seem to justify such an effort. Basically, if changes in phenotype of commonly used strains of laboratory rodents were occurring, we would see it in the existing data. If adverse events were occurring in control animals, a properly conducted study would report these adverse effects and we would see these changes in behavior of control animals in the literature. There are also ethical and legal obligations for reporting such adverse events to the veterinary staff and institutional ethics boards for animal research. Furthermore, the question of why the control mice are behaving differently than all other control mice would be very interesting research question that scientists would follow up on.

The authors of this study are searching for an answer to a non-existent problem. All Séralini had to do is a literature search to determine if this is a problem. They are trying to blame external factors (chemical contamination and GMOs) for a problem of genetics. We can, in fact, address many of the issues that authors say cannot be addressed by mining the very data that Seralini and colleagues want to throw away out of hand. But they didn't address them and thus cannot make any conclusion except that genetically

engineered crops and low levels of these chemicals exist in laboratory feed.

The authors also conclude that because of the high background pathology (reminder: not demonstrated here), the recommendation to study larger groups of animals is invalid. This is not how statistics works. If your variation is higher, you need a larger group to discern a pattern. If there is, in fact, high background variation, the only thing this underscores is the important of choosing an appropriate mouse strain for your study.

Overall, this paper is a thinly veiled attempt to address the consensus scientific criticism of Séralini's previous work. This new paper doesn't do anything to help his case that these criticisms were not valid.

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