

Genetic Engineering Against Alzheimer



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1. Preface

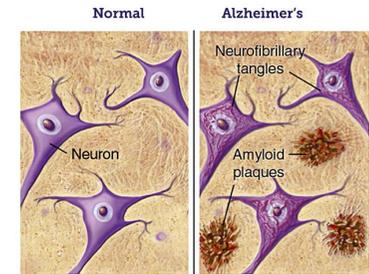
Only in Switzerland, there are approximately 150'000 people suffering from dementia.¹ And according to a report from Alzheimer's disease International, there are 46.8 million people worldwide suffering from dementia. The Alzheimer-disease is with two-thirds of all cases the most common form of dementia.²

This is currently a very important issue in scientific research but also in our society. Eventually anyone is going to encounter this brain disease through family, friends or even through yourself. Unfortunately, this brain disease is still considered as incurable. If we are not going to make any progress with treatments and preventions of the Alzheimer-disease, the number of affected people is going to increase persistently.

As we are both interested in chemical and biological experiments also involving medicine, we decided to focus on this rather important topic. We asked ourselves if there have been any experiments with genetically engineered animals or patients to combat this disease. We also want to know what kind of methods or techniques have been used in these experiments. We're also curious to know whether these attempts in fighting the Alzheimer-disease has made any progress or has even been successful.

2. Introduction

The Alzheimer's disease was discovered in the year 1906 by Alois Alzheimer³, who examined a 50-year-old woman who suffered from sleeping problems, paranoia, aggression, and memory loss. When she died, he analyzed and colored slices of her brain to find the cause of her illness. Alois Alzheimer found two different types of accumulations, which are nowadays known as "plaques" and "tangles".⁴



Picture 1:
<https://www.brightfocus.org/alzheimers-disease/infographic/amyloid-plaques-and-neurofibrillary-tangles>

These days Alzheimer is the most common case of dementia and many people have to deal with it. It is predicted that there will be 100 millions of people suffering from Alzheimer by the year 2050.⁵ That should be a motivation for scientists and research groups to continue searching for a solution.

But until now, there isn't a cure for Alzheimer's disease. Certainly, many research groups are trying their best, but so far there are only treatments which ease the severity of the symptoms and improve the quality of the life of an Alzheimer patient. There isn't any medication which actually works against this disease and also genetic engineering only had little success in finding an efficient method for preventing and healing Alzheimer.

To find a cure for Alzheimer, some experiments with humans are done, but most experiments are conducted with animals. Although 99.6% of all the medication, which works for animals with Alzheimer, failed when they were tested on people with Alzheimer.⁶ Despite the fact that these numbers are known, many different research groups in different places conducted experiments with mice to figure out if they are able to find a cure. In this process they changed the mice genetically so that they became dement. After achieving that, they tried to find an active agent or procedure to remove the illness again. Their goal was to reverse the memory loss of Alzheimer patients who still are in an early phase of the disease.

Naturally there are many people who are strictly against animal experiments and who are looking for alternative methods. But sadly, animal experiments are necessary and can't be replaced by a computer-operated trial, human experiments, or anything else. It is the law that medication needs to be tested on animals before it is tested on humans.⁷

¹ <http://www.alz.ch/za/index.php/zahlen-und-fakten-zur-demenz.html> (06.03.2019)

² <https://www.alzheimer-forschung.de/aktuelles/meldung/weltweit-468-millionen-demenzranke/> (06.03.2019)

³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3181715/> (13.03.2019)

⁴ https://www.alzheimer-synapsis.ch/fileadmin/user_upload/PDF/Artikel_StandAlzheimerForschung_Monard.pdf

⁵ https://www.alzheimer-synapsis.ch/fileadmin/user_upload/PDF/Artikel_StandAlzheimerForschung_Monard.pdf (06.03.2019)

⁶ <https://www.pcrm.org/ethical-science/animals-in-medical-research/alzheimers-disease-research-without-animals> (13.03.2019)

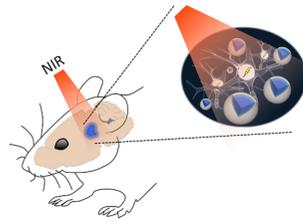
⁷ <https://biotechlemcenter.interpharma.ch/2189-tierversuche> (27.03.2019)

3. Description of experiments

In scientific research, there have been various experiments hoping to discover a cure for the Alzheimer-disease. They have conducted experiments with humans, apes, and rodents. We will mainly focus on the animal experiments with mice and we will discuss two chosen experiments more in detail.

- 1) The first experiment we would like to address was conducted at the Edith Cowan University in Australia. The discovery of this experiment is seen as a revolution for the Alzheimer research. In this experiment they used a specific genetic engineering technique called 'optogenetics'. To make sense of this procedure, the neuroscientific technique must be explained first.

With optogenetics you can control neurons by using light or a laser beam. They extract a gene from a light-sensitive protein, called channelrhodopsin. This protein is naturally found in algae and microbes. This gene is inserted into a specific neuron in the brain. When channelrhodopsin is exposed to laser light with a specific wavelength, it will open an ion channel in the membrane of the neuron and the neuron will transmit electrical signals. By turning neurons on and off, we can control people or animal's behavior but the main intention of optogenetics is to reveal how the brain functions.⁸



Picture 2: <https://www.the-scientist.com/daily-news/dbs-with-nanoparticle-based-optogenetics-modifies-behavior-in-mice-30303>

In the Alzheimer research, they used a laser beam to stimulate the neuron, which is responsible for recalling memories, and reactivated it. And as a matter of fact, when this technique is applied to mice, they responded successfully and recalled memories. This genetic engineering technique cannot be applied on humans yet since it's still not fully researched. Through this discovery, Alzheimer drugs could be developed to reactivate neurons in the brain to restore the patient's memory.⁹

⁸ <https://cosmosmagazine.com/biology/optogenetics-understanding-the-brain-one-flash-of-light-at-a-time> (13.04.2019)

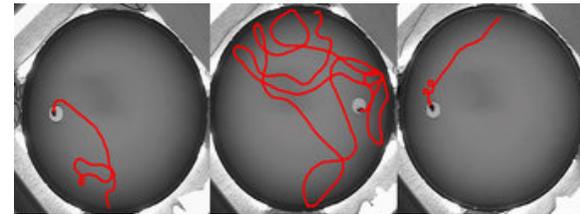
⁹ <https://ch.galileo.tv/science/erste-tests-erfolgreich-alzheimer-mauesen-wurden-erinnerungen-zurueckgegeben/> (14.04.2019)

- 2) The second experiment was conducted at the Max Planck Society. The characteristic trait of the Alzheimer disease is the deposits of the amyloid beta and the tau protein. The protein amyloid beta forms insoluble clumps between the nerve cells and the tau protein, which is responsible for the transport in cells, clumps inside the neurons. As a result, the nutrient transport stops working, and this is the beginning of memory loss. In experiments with mice, they were able to show that the harmful effect of the tau protein disappears, when the corresponding tau gene is turned off. Now, scientists are testing drugs on mice that prevents the deposits of the tau protein.¹⁰

But how do research groups measure the memory loss on mice?

While working on this project we've read about two different tests to examine the mice's ability to remember something. One of them is the swimming test. The mice are put in a pool of water and a healthy animal quickly finds the rescuing platform lying below the surface while the transgenic mice takes four times as long and aimlessly paddles through the pool until they find the platform.

The second test is the lemon scent test. The scientists spray lemon fragrance on the mice while giving them minor electric shocks. After a while, the healthy animals show a frightening behavior to the lemon odor because of the electric shocks. The mice with the Alzheimer-disease do not show this behavior as they keep forgetting the meaning of the lemon scent.¹¹



Picture 3: Memory loss swimming test
https://www.mpg.de/1156818/alzheimer_gedaechtnis

¹⁰ https://www.mpg.de/1156818/alzheimer_gedaechtnis (16.04.2019)

¹¹ <https://ch.galileo.tv/science/erste-tests-erfolgreich-alzheimer-mauesen-wurden-erinnerungen-zurueckgegeben/> (16.04.2019)

4. Interview

Unfortunately, our interview partner's company did not allow her to send us any pictures from the laboratory and we were also not allowed to publish her name.

1. Why are animal experiments conducted?

Of course, we try to conduct as little experiments with animals as possible, but sadly, there are not many different alternatives which could be used for further research. However, we are supporting and financing the development of alternative methods. Animal experiments are very complicated to execute and always need a lot of time. Besides that, they are very expensive, and many people scrutinize the ethical aspects of animal experiments. Those were just a few reasons why we try to perform as little animal experiments as possible, but the use of laboratory animal is indispensable for our future.

2. Do you think that experiments to find a cure for the Alzheimer disease should be conducted on humans?

In Germany there is a law that determines that new methods and medications need to be tested on animals first, and only when these experiments are successful, they are tested on people. There are research groups which are already testing medication on Alzheimer patients, and I think that there will be more experiments on humans in the future, if science continues to make progress and we achieve more positive results from animal experiments.

3. Why are mice mostly used for these experiments and where are they from?

Mice are used for these kinds of experiments because 95% of the genes in a mouse occur in humans with a similar structure. Animals like pigs and sheep are bought at farms. But for example, mice used for animal testing are bred to only serve for experiments.

4. Do mice suffer during these experiments?

The research and animal testing includes experiments which could cause pain, suffering or harm for an animal. But if experiments on mammals could impact the animal's well-being, they need to be authorized first.

5. Are there any rules which have to be obeyed for conducting animal experiments?

Yes, indeed, Germany follows some of the strictest regulations in the world. The German Animals Welfare Act provides extensive protection for the animals. While animal testing is unequivocally allowed, it can only be performed when at least one of the four criteria for animal testing is fulfilled. An example for such a criteria is, that the experiment is crucial for basic research.

5. Discussion

With genetic engineering we are on a good way to find a cure for Alzheimer's disease and many other illnesses. But until now, there isn't a medication or procedure for the healing of Alzheimer, which means we didn't quite reach our goal yet.

In the experiments with mice, which we described in our paper, researchers have found solutions for animals with Alzheimer, but different attempts show that most of these don't actually work for humans with Alzheimer. That's why more experiments should be conducted on humans in the first place. The animal experiments cost a fortune and in the end they don't give us valuable and proper solutions for fighting Alzheimer in humans.¹² So why should we continue using and even harming animals like mice or monkeys in experiments, which eventually aren't even of prime importance?

One answer to this question is the fact, that it is the law. We need to test medication on animals first, before we can test it on humans.¹³ And naturally, in a few sections of medical research, animal experiments were, and still are, very important for research. With animal experiments we can examine the cause of a disease and test different treatments and also investigate the safety and efficiency of medication. But for an illness like Alzheimer, where animal experiments lead to nothing, they are just a waste of money and time.

As already mentioned, luckily there are not only animal experiments, but also experiments conducted with humans. Between 2002 and 2012, there were over 200 clinical trials with 244 different drugs conducted worldwide.¹⁴ Many Alzheimer patients, but also healthy people, volunteered for this process. And there were many moments in which they thought that they found a cure, but eventually a promising medication either had too many side effects or didn't work properly on all patients. We think that there will be more experiments on humans in the future, because the scientists are starting to realize that some drugs may be effective in animals, but not in humans. Human experiments are crucial and necessary for an approval of a new medication, but naturally not many people want to endanger their health and life for clinical experiments. Human experiments need to be approved by the ethics committee and, here in Switzerland, by Swissmedic.¹⁵ And logically there needs to be some evidence to prove that a method or medication isn't too risky, so that people volunteer for experiments. And this evidence is established with animal experiments.

¹² <https://www.peta.org/blog/alzheimers-researchers-admit-experiments-animals-big-fat-failure/> (04.05.2019)

¹³ <https://biotechcenter.interpharma.ch/2189-tierversuche> (05.05.2019)

¹⁴ <https://alzheimer.ch/de/wissen/forschung/magazin-detail/466/das-geschaft-mit-der-hoffnung/> (04.05.2019)

¹⁵ https://swissethics.ch/doc/swissethics/manual_research_nov2015_d.pdf (04.05.2019)

6. Summary

Alzheimer is a common illness and people are exposed to this disease almost on a daily basis. Through this paper, we learned what the cause of Alzheimer is and how science has tried to find different treatments for the disease. We explained two techniques which conducted experiments with transgenic Alzheimer-mice. One experiment used optogenetics to control the neurons responsible for activating memories and the other one turned off the corresponding tau gene to prevent the harmful effect of the tau protein. In both experiments, the scientists measured the memory loss of mice and discovered that the mice could retrieve their memories. But both experiments aren't advanced enough to be tested on humans.

Many people think, that animal testing should be forbidden by the law. But as we found out in our interview, many regulations and rules need to be followed for conducting such experiments. Nowadays, animal experiments are irreplaceable. That's because we didn't find a good alternative until now. But scientists are still researching and looking for an alternative solution. The law states, that new medication needs to be tested on animals first, and only when they were successful, they can be tested on humans.

We think, that finding a prevention or treatment for Alzheimer is very important, because the illness is constantly spreading. Our conclusion is, that animal experiments aren't substitutional in several studies and it is the law that these experiments need to be done. But nevertheless, we should try to stress the animals as little as possible and minimize the number of animal experiments.

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