Restoring Public Trust in Science and Clearing Up Misconceptions about Alzheimer's Disease Controversies

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Scientific research is supposed to be conducted in pursuit of the truth while maintaining high ethics and standards to allow for trust between scientists and the public. There is a level of rigor that is expected to have been performed when a novel drug comes to market or a major advancement in science is announced. However, in the past few years, that notion has been challenged because of the falsification of data published about Alzheimer's disease (AD), which is the most common type of dementia. In 2022, about 6.5 million Americans were estimated to be living with AD, whereas a predicted 14 million Americans will be living with AD by 2060 (Kumar, 2021). One of the many hypotheses for what causes AD to develop is the aggregation of amyloid beta (Ab) plaque in the hippocampus and cortex of the brain. It is believed that these aggregates form tangles in the extracellular space between neurons in the brain leading to neuronal degeneration.

The work in question was done by Sylvain Lesné and published in Nature in 2006. Having amassed nearly 2300 citations as of writing, it was one of the most widely cited papers in the field up until the discovery of tampered images within the publication. The paper allegedly found that an isoform of Ab, called Ab56, was correlated with memory deficits in a strain of TG2576 mice. Western blot data (which is an experiment utilized by scientists to detect the presence and concentration of a protein) was critical to the determination of the fabrication by piecing together images from different experiments (Piller, 2022).

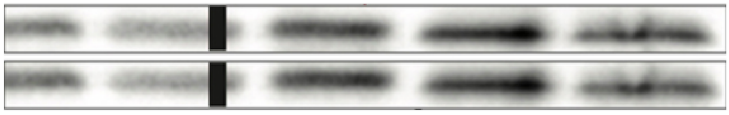

Figure 1. The duplication of bands for different western blotting experiments Piller, C. (2022).

It was also found that some bands appeared duplicated from other experiments. This falsified work led to media headlines and articles about how the entire Ab theory of AD was discredited. When in actuality, very few people continued to work on Ab56 and worked on Ab oligomers of different sizes. It also broke the public's confidence in Ab research and tarnished the credibility of any future work in the field. The amyloid theory for AD was given a smudge on its record; however, the theory itself was not invalidated by this specific paper and its fabrications. Since 2006, many papers have come out looking at Ab of different lengths and functions, which in turn, have found correlations to memory loss (Gu & Guo 2013).

The future of AD research is still promising even after the notorious mishap. Most of the Ab therapies are now targeting different isoforms of Ab called Ab40 and Ab42. Several drugs have been approved by the FDA in recent years. For instance, in 2021 Aducanumab was approved as an amyloid beta-directed antibody. However, later that year, safety data was published showing that 1/3 of patients had developed amyloid-related imaging abnormalities (ARIA) (Ebell & Barry, 2022). The abnormalities result in small lesions throughout the brain which can result in swelling and bleeding in the brain causing headaches and nausea (Ebell & Barry, 2022). It was successful in decreasing the Ab plaque present which was long sought in the field. AD research is taking the direction that utilizes genetic editing to target genes linked to the production of Ab. In 2021, researcher Yangyang Duan published his work in Nature Biomedical Engineering where he used CRISPR-Cas9 (the first edition CRISPR editing system) to cause a disruption in the AB pathway (Dunn et al., 2021). They used a single intravenous injection which is an improvement compared to the monthly injections required by the antibody treatments. This is because one injection should decrease the price of treatment compared to the monthly injections. Through this experiment, they saw a decrease in Ab plaque burden and an increase in cognitive performance in an aggressive mouse model. This is a very promising start for gene editing's use for treating neurodegenerative diseases.

Alzheimer's Disease is a complex neurodegenerative disorder that we still have a lot to understand about how it develops and how it may be treated. Targeting Ab is a possibility for treatment but should not be our sole focus. Moving forward, science must be conducted in the pursuit of truth and not in the pursuit of a publication. In following this, the scientific community may make progress in regaining the public's trust in science that has been severely degraded in recent years.

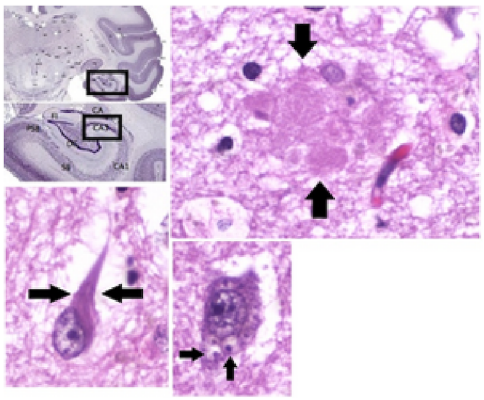

Figure 2. The pathology of AD showing the Ab plaques and tangles in the hippocampus of the brain. Wikimedia Commons Mikael Häggström (2020).

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