THE Science BREAKER
SCIENCE MEETS SOCIETY

DATE ##, 2017

Evolution & Behaviour

The mutation that allowed our brain to grow

by Reinier Prosee[1] | PhD student

[1]:Department of Molecular Biology, Section of Biology, Faculty of Science, University of Geneva, Switzerland

This Break was edited by Carlos Rivera Rivera, Scientific Editor - TheScienceBreaker

During human evolution, one of the most remarkable events was the expansion of the upper layer of the brain: the so-called neocortex. This event took place about 2 million years ago and allowed us to develop the cognitive abilities that characterize modern day humans. In a recent paper published in the scientific journal *Science,* the geneticist Marta Florio and her colleagues pinned down a single genetic event that could help explain this sudden expansion of the neocortex. They identified a gene, called ARHGAP11B, which is present in our DNA but also in that of most humanoid species like, for example, the chimpanzee. This gene affects the generation and division of brain cells in a specific part of the neocortex. In this part of the brain there is sufficient room for cell growth, which means that it can support rapid brain expansion.

DNA and genes are sequences of molecules called nucleotides. There are four different nucleotides, which are represented by the letters A, C, T, and G -and specific combinations of these nucleotides encode for specific genes. Genes are the recipes for proteins, and proteins, in turn perform most of the essential tasks in a cell, and indeed, in the whole body. The gene described in this study, *ARHGAP11B,* is actually a duplicate of another gene that is more widespread in the tree of life: *ARHGAP11A.* This gene codes for a protein that is important for the communication between cells. Because this is a basic and essential cellular function, the gene is almost identical in other organisms, a phenomenon called evolutionary conservation.

As mentioned above, genes are sequences of nucleotides. The sequences that encode a gene, however, are not continuous: there are pieces of non-important sequence in between the important pieces. It is like reading an interesting article in a magazine that places advertisements every other page. The chunks of sequence in a gene that encode for a protein are called "exons", because they are important for the expression of the protein, and the non-important pieces in between them are called introns. The "original" *ARHGAP11A* gene consists of 12 exons, the parts that will be translated into the protein, but some of these were lost during the course of evolution in the "copy" gene, *ARHGAP11B*. To be more precise, our current *ARHGAP11B* gene is only read until the end of exon 6, in contrast to the end of exon 12 in the original gene.

By looking at the DNA sequence of both *ARHGAP11A* and *-B* it is clear that the sequence is almost identical, especially in the protein-coding exons. One exception is a single nucleotide ("letter") in exon 5: a C that is substituted for a G. At first sight this seems like a minor change, but in fact this single nucleotide completely changes the way the protein is made. In fact, the structure of a big part of the protein now becomes very different and unique to humans. An earlier study already determined that this new version of the protein changes its original function and that this particular change gives brain cells in the neocortex the opportunity to grow and divide at an unprecedented level.

Based on sequence information available for closely related non-human primates, Marta Florio and her team could show that, in all other primates, the *ARHGAP11B* gene lacks the conversion from C to G in exon 5, confirming it to be a human-specific event. The next thing to do was to test the effects of the different versions of the gene, encoding slightly different

proteins, on animal development. The different varieties of the *ARHGAP11B* gene, one with and one without the C to G conversion, were introduced into mouse embryos, and their brain development was closely examined. As expected, more dividing cells were observed in the neocortex of mice that had received the human-specific *ARHGAP11B* gene.

From all this, the conclusion is that a seemingly simple conversion from C to G in exon 5 of *ARHGAP11B* has led to a human-specific protein structure that changed its function. While it lost its original function, it gained an important role in allowing specific brain cells to grow and divide allowing the expansion of the neocortex. This is regarded as one of the key steps in the development of our current cognitive abilities.

The molecular mechanisms by which the protein supports this function are still unknown, so this will undoubtedly be a topic of future research. Also, it is unlikely that this protein is solely responsible for the expansion of our neocortex. It is probably one of multiple (yet unidentified) key players, but this shouldn't obscure the importance of the present study. It shows us how a minor genetic change has had widespread effects even altering the course of human evolution.