**How the domestic rabbit became fearless**

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The domestication of animals is a gradual process in which wild animals become genetically modified and adapted for a life in captivity. This transition from wild to captive environments is mediated through several phenotypic modifications affecting behaviour, appearance, physiology and reproduction. The most striking of these modifications is tameness, which is a common feature of all domesticated animal species and includes reduced aggression and increased fearlessness towards humans when compared with their wild ancestors. An important and mostly unresolved question is which type of genetic changes that result in tame behaviour and how these alterations affect brain function. A deeper understanding of the biology of tame behaviour in domestic animals may also be a model for how human variation in brain morphology affects behavioural responses.

In a paper published in the Proceedings of the National Academy of Sciences (USA) on June 25, 2018 we report that there are morphological differences between brains from wild and domestic rabbits. Wild rabbits have a very strong flight response. In nature, this evolved as a direct consequence of predation and is essential for survival. In contrast, most domestic rabbits are docile and exhibit a strongly attenuated flight response. This striking shift in behaviour was highlighted by Charles Darwin in The Origin of Species: “Hardly any animal is more difficult to tame than the young of the wild rabbit; scarcely any animal is tamer than the young of the tame rabbit.”

This difference between wild and domestic rabbits is to a large extent genetically determined. If one raises wild and domestic rabbits under similar conditions there are still very striking behavioural differences reflecting a genetic basis. These genetic differences have accumulated in domestic animals due to the man-made selective breeding ever since rabbits started to be kept in captivity more than a thousand years ago. In a previous study, we determined the DNA sequence of all genes from many wild and domestic rabbits and searched for consistent differences between the two groups. This work demonstrated that genetic changes between wild and domestic rabbits are particularly common in genes that play a role during brain development. As a natural follow-up to this previous study, we now used high-resolution magnetic resonance imaging (MRI) to address the question whether these genetic changes have affected the general organization of the brain.

We raised eight domestic and eight wild rabbits under very similar conditions to minimize differences in behaviour simply due to environmental or social effects. The brain MRI data were interpreted with sophisticated image analysis and we report three profound differences. Firstly, domestic rabbits have a smaller brain-to-body size ratio than wild rabbits, a difference that has been previously documented in several other domestic animals. Secondly, domestic rabbits have a reduced amygdala and an enlarged medial prefrontal cortex. Thirdly, there was a generalized reduction in white matter structure in domestic rabbits. These differences in brain morphology make perfect sense in relation to the fact that domestic rabbits are less fearful and have an attenuated flight response as compared with wild rabbits. This is because the amygdala, which is involved in sensing fear, is smaller in size while the medial prefrontal cortex, controlling the response to fear, is larger in domestic than wild rabbits. The change in white matter structure suggests that domestic rabbits have a hampered communication within and between brain hemispheres. This may explain why domestic rabbits are slower in reacting and more phlegmatic than their wild counterparts.

The results of the present study were surprising because they revealed pronounced differences in the organization of the brain, which was unexpected since wild and domestic rabbits have only diverged for a relatively short period time. No previous study in domestic animals has explored changes in brain morphology in such a depth as done in this study, but we hypothesize that similar changes in brain morphology will very likely be present in other domestic animals. Does this result have implications for human biology? Our behavioural responses are heavily influenced by our experiences throughout life, but our rabbit data strongly supports the notion that differences in our genetic constitution have an important impact on how we sense and handle fear, similar to the relationship between genetics, brain morphology and behaviour as now established in the rabbit.

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