Selfdomestication Homo Sapiens

Review by Daniël Verhoeven

Introduction

European hunter-gatherers "domesticated" dogs from wolves some 20,000 to 30,000 years ago[1]. They did not live in houses. Ditto for the first sheep domesticated by nomadic shepherds in Mesopotamia. Based on this knowledge, we now know that the word 'domestication, does not cover it. There is no 'domus' involved. Let's just say that 'domestication' is a metaphor. Just as 'download' is a metaphor for moving computer files from one computer to another. Not to be taken literally.

The evolution of that domestication was different in humans than in animals. Humans chose to do that at some point in prehistory, even if it was not really with deliberate or intentional intent. But the term 'domestication syndrome' is used for both processes, domestication and self-domestication.

In animals, it is an artificial process, possibly preceded by a change in animal behaviour possibly the result of an accidental mutation. Animals did not offer themselves for some domestication experiment. But wild animals, already somewhat tame due to a mild genetic mutation, sought the company of humans. Probably in search of food. Those people then took advantage of that opportunity to further select those animals for tameness, i.e. selective breeding.

An interdisciplinary team of researchers showed that hyper-methylation in the regulatory region of the BAZ1B gene reduced the aggression of human carriers[2]. These were therefore given preference in mate choice. Their offspring eventually supplanted the aggressors. "Selection against bullies"[3]. Not artificial selection like pets, but sexual selection.

Sexual selection is described by Darwin in 'The Descent of Man, and Selection in Relation to Sex'[4]. Sexual selection, in biology, is the selection of mates based on traits perceived to be attractive. Such traits make it easier to get a mate. Sexual selection is similar to natural selection in that it ensures that animals with these traits can have more offspring. In animals, it is therefore a driving mechanism behind biological evolution. Note that with sexual selection, 'natural selection' also

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1 Callaway, E. Prehistoric genomes reveal European origins of dogs. Nature (2013). https://doi.org/10.1038/nature.2013.14178, <https://www.nature.com/articles/nature.2013.14178>.

2 Zanella, Matteo et al., Dosage analysis of the 7q11.23 Williams region identifies BAZ1B as a major human gene patterning the modern human face and underlying self-domestication. Sci. Adv.5, eaaw7908 (2019). DOI:10.1126/sciadv.aaw790 https://pmc.ncbi.nlm.nih.gov/articles/PMC9473395/8. <https://www.science.org/doi/10.1126/sciadv.aaw7908>.

3 B. Hare, Survival of the friendliest: Homo sapiens evolved via selection for prosociality. Annu. Rev. Psychol. 68, 155–186 (2017). <https://www.annualreviews.org/content/journals/10.1146/annurev-psych-010416-044201>.

4 Darwin, Charles (1871). The Descent of Man, and Selection in Relation to Sex. Vol. 1 (1st ed.). London: John Murray. ISBN 978-0-8014-2085-6. Retrieved 18 June 2009. <https://darwin-online.org.uk/EditorialIntroductions/Freeman_TheDescentofMan.html>.

remains in play. If the offspring of the happy couple die before they have offspring of their own, it is also the end of the story.

In 1963, Dmitry Belyayev and Lyudmila Trut set up experiments to domesticate the silver fox at the Institute of Cytology and Genetics in Novosibirsk in Russia. An experiment that lasted 50 years and produced numerous generations of silver foxes. Belyaev suggested in 1979 that reduced stress levels in animals living in protected anthropogenic environments caused multiple changes in hormonal responses and that these reset gene expression patterns.

In 2014, Adam Wilkins, Richard Wrangham and Tecumseh Fitch pointed out the crucial role of mild deficits of 'neural crest cells' (NCC) in embryogenesis in domesticated animals. These NCC migrate to different sites in the body as the foetus continues to develop (multiply and specialise). The authors made a diagram (Figure 1) of this migration[5].

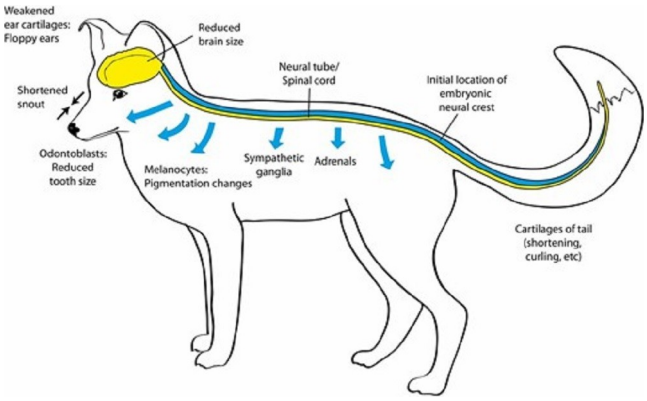

Figure 1: Developmental diagram of the "domestication syndrome" in relation to the neural crest. The blue tube indicates the approximate position of the neural crest in the early embryo and the blue arrows indicate the migration pathways of the neural crest cells. Cortesy Genetics Society of America.

They argue that the genetic basis of impaired function of 'neural crest cells' are genetic changes with a moderate, quantitative effect. That reduction did have a plethora of phenotypic consequences in domesticated animals: increased docility and tameness, coat colour changes, reduced tooth size, changes in the morphology of skull and muzzle, changes in ear and tail shape more frequent and non-seasonal fertility cycles, changes in adrenocorticotropic hormone levels, altered concentrations of various neurotransmitters, prolongation of growing-up behaviour and reductions in both total brain size and certain brain regions[6].

5 Wilkins, Adam S, Richard W Wrangham, W Tecumseh Fitch, The “Domestication Syndrome” in Mammals: A Unified Explanation Based on Neural Crest Cell Behavior and Genetics, Genetics, Volume 197, Issue 3, 1 July 2014, Pages 795–808, https://doi.org/10.1534/genetics.114.165423, <https://academic.oup.com/genetics/article/197/3/795/5935921>.

6 Wilkins, Adam et al., 2014.

By comparing fossils of Homo sapiens with their archaic ancestors, archaeologists have observed many of the same telling phenotypic features that arise as a result of self-domestication in animals. These features include reduced sexual dimorphism, smaller teeth, skull reduction and a smaller body. Fossils of Homo sapiens also showed the flattening of the eyebrow arch projection and flatter faces[7]. Selfdomestication still had to be demonstrated with humans and this was done by the team of Matteo Zanella in 2019[8].

Results of their research

Whereas Dmitry Belyayev and Lyudmila Trut still had to breed silver foxes for their experiments, in the third millennium researchers work with organoids from human stem cells. The interdisciplinary team[9] that analysed the auto-domestication of Homo Sapiens consisted of sixteen researchers from different disciplines: stem cell research, biology, genetics, epigenetics, medicine, complex systems and linguistics. At the time, the researchers were working in Spain, Italy, Germany, Switzerland, which does not mean that they were from those countries. For example, linguist and expert complex systems Cedric Boeckx, is has a Belgian origin.

Previous research had already shown that in humans with Williams-Beuren syndrome, the same phenotypic features came into view as in domesticated other mammals, such as craniofacial dysmorphisms, pronounced friendliness and reduced reactive aggression. It was also soon clear that these were also related to deficits of the neural crest[10] [11] [12].

> “Williams-Beuren syndrome [WBS; OMIM (Online Mendelian Inheritance in Man) 194050] and Williams-Beuren region duplication syndrome (7dupASD; OMIM 609757), caused respectively by the hemideletion or hemiduplication of 28 genes at the 7q11.23 region [WBS critical region (WBSCR)], represent a paradigmatic pair of neurodevelopmental conditions whose NC-related craniofacial dysmorphisms and cognitive/behavioral traits (6, 7) bear directly on domestication-related traits relevant for AMHs (facial reduction and retraction, pronounced friendliness, and reduced reactive aggression) (fig. S1A). Structural variants in WBS genes, for example in the case of GTF2I and its paralogs, have been shown to underlie stereotypical hypersociability in domestic dogs and foxes (8, 9).[13]”

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7 Wrangham, R. W., 2019, Hypotheses for the Evolution of Reduced Reactive Aggression in the Context of Human Self-Domestication, Front. Psychol., 20 August 2019, Sec. Evolutionary Psychology, Volume 10 - 2019 | https://doi.org/10.3389/fpsyg.2019.01914, <https://www.frontiersin.org/journals/psychology/articles/10.3389/fpsyg.2019.01914/full>.

8 Zanella, Matteo et al., 2019.

9 Zanella, Matteo et al., 2019.

10 Pober BR. Williams-Beuren syndrome. N Engl J Med. 2010 Jan 21;362(3):239-52. doi: 10.1056/NEJMra0903074. Erratum in: N Engl J Med. 2010 Jun 3;362(22):2142. PMID: 20089974. <https://pubmed.ncbi.nlm.nih.gov/20089974/>.

11 B. M. vonHoldt, E. Shuldiner, I. J. Koch, R. Y. Kartzinel, A. Hogan, L. Brubaker, S. Wanser, D. Stahler, C. D. L. Wynne, E. A. Ostrander, J. S. Sinsheimer, M. A. R. Udell, Structural variants in genes associated with human Williams-Beuren syndrome underlie stereotypical hypersociability in domestic dogs. Sci. Adv. 3, e1700398 (2017).

12 A. V. Kukekova, J. L. Johnson, X. Xiang, S. Feng, S. Liu, H. M. Rando, A. V. Kharlamova, Y. Herbeck, N. A. Serdyukova, Z. Xiong, V. Beklemischeva, K. P. Koepfli, R. G. Gulevich, A. V. Vladimirova, J. P. Hekman, P. L. Perelman, A. S. Graphodatsky, S. J. O’Brien, X. Wang, A. G. Clark, G. M. Acland, L. N. Trut, G. Zhang, Red fox genome assembly identifies genomic regions associated with tame and aggressive behaviours. Nat. Ecol. Evol. 2, 1479–1491 (2018).

13 Zanella, Matteo et al., 2019.

These deficits are located in the 7q11.23 zone (WBSCR) where alterations were detected in 28 genes. The BAZ1B gene plays a central role. Most people have two copies of this gene. Curiously, one copy of BAZ1B, along with a handful of others, is missing in people with Williams-Beuren syndrome. The researchers also found in anatomically modern humans a large convergence between BAZ1B control and adaptations of genes that modify neural crest regulation[14].

To find out whether BAZ1B played a role in these facial features of Homo Sapiens, they cultivated eleven neural stem cell lines: four from people with Williams-Beuren syndrome, three from people with a different but related disorder in which they have duplicates rather than deletions of the disorder's major genes, and four from people without either disorder.

They then used different techniques to adjust BAZ1B activity up or down in each of the stem cell lines. They found that these adjustments affected hundreds of other genes known to be involved in facial and cranial development.

Overall, they found that a weakened BAZ1B gene led to the prominent facial features of people with Williams-Beuren syndrome, suggesting the gene plays an important role in facial development. They also found that BAZ1B regulates the neural crest epigenome in a dose-dependent manner.

With these data, they compared databases of the native state of the BAZ1B gene in archaic Neanderthal and Dinosovans:

> "For this, we carried out a systematic integrative analysis of the overlaps between our empirically defined BAZ1B dosage–sensitive genes (blue Venn in Fig. 4B) and a combination of uniquely informative datasets highlighting differences between modern humans and archaics (Neanderthals/Denisovans) (represented in Fig. 4A by skulls illustrating the more “gracile” and “juvenile”profile in AMH relative to Neanderthals visible in the overall shape of the neurocranium, reduced prognathism, brow ridges, and nasal projections) (1, 13–15).[15]

When the researchers looked at those hundreds of BAZ1B-sensitive genes in modern humans, two Neanderthals and a Denisovan, they found that those genes had undergone a host of regulatory mutations in modern humans themselves. This suggested that natural selection had given them their current shape. And since many of these same genes have also been under selection in other domesticated animals, modern humans also underwent a process of domestication, the team of researchers reported. The scope of this discovery cannot be underestimated, according to the researchers:

> “Last, it is noteworthy that genes implicated in NC development also play significant roles in the establishment of brain circuits that are critical for cognitive processes like language or theory of mind prominently affected in 7q11.23 syndromes. Among the genes downstream of BAZ1B that we uncovered in this study, FOXP2, ROBO1, and ROBO2 have long been implicated in brain wiring processes critical for vocal learning in several species (50, 51), including humans, and will warrant further mechanistic dissection in light of the distinctive linguistic profile of WBS individuals.”[16]

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14 Zanella, Matteo et al., 2019.
15 Zanella, Matteo et al., 2019.
16 Zanella, Matteo et al., 2019.

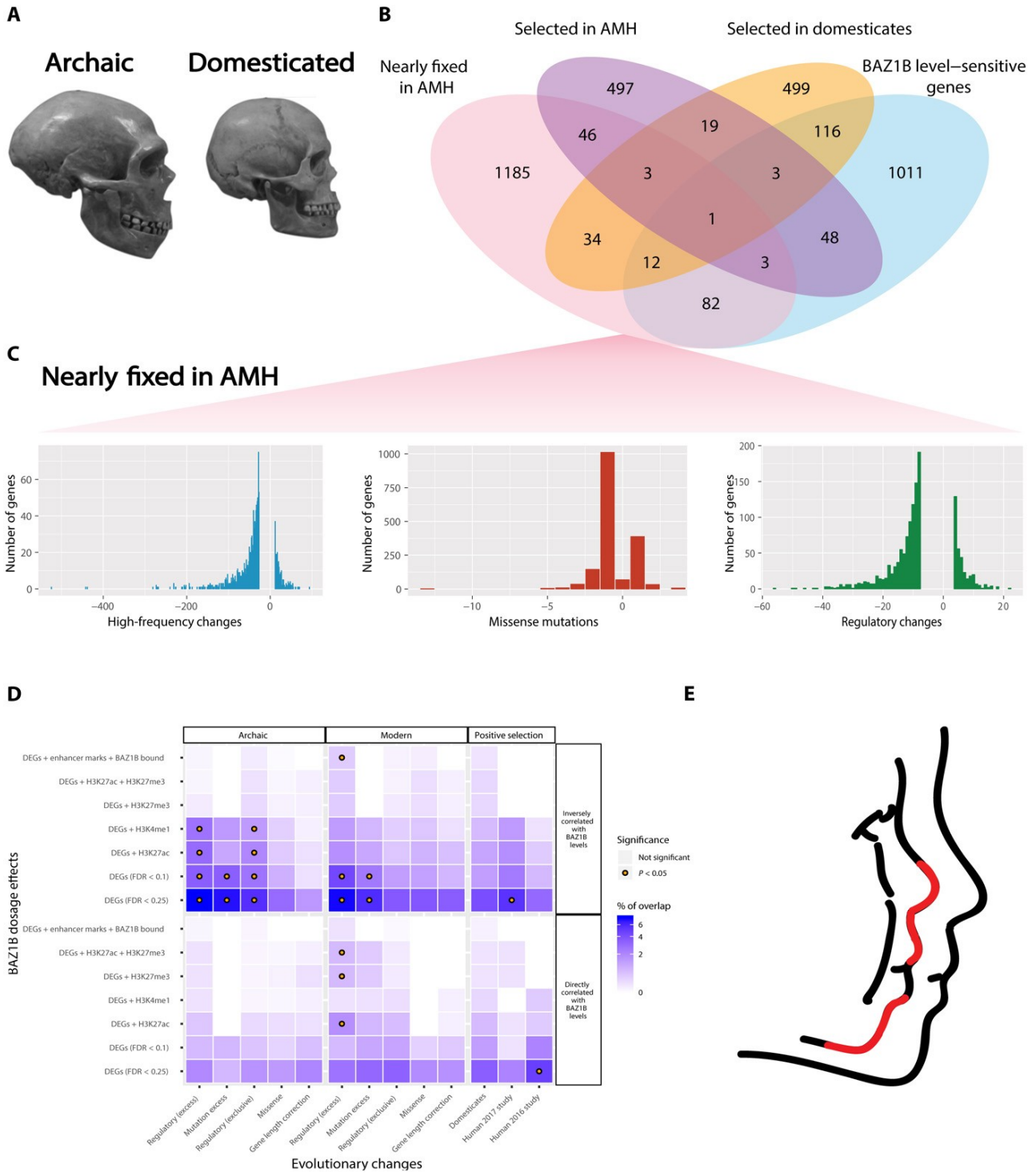

*Figure 2: BAZ1B KD impairs migration and induction of patient-specific iPSC-derived NCSCs.(A) Schematic representation of the KD strategy on our iPSC-derived NCSC cohort. (B) BAZ1B mRNA levels in all the interfered lines (scr, sh1, and sh2) as measured by qPCR. Data represent aggregates of samples with the same number of BAZ1B copies (7dup, CTL + atWBS, and WBS). Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) is used as a normalizer. (C) Eight- and 16-hour time points from the wound-healing assay analyses performed on a 7dupASD and a WBS NCSC line upon BAZ1B KD. Cells from the same line infected with the scr sh were used as references for the migration (n = 2). (D) Days 7, 10, and 12 of NC differentiation from embryoid bodies (EBs) of an scr-interfered iPSC line and its respective BAZ1B KD (n = 3). (E) mRNA levels of NC markers at day 12 of differentiation in three individual experimental replicates [bright-field images are reported in (D)]. An iPSC line is included as a negative control. Student's t test was used (ns, not significant; *P < 0.05, **P < 0.01, ***P < 0.001, and ****P < 0. 0001), Courtesy Science Advances,https://www.science.org/doi/10.1126/sciadv.aaw7908*

This had shown that not only was the shape of Homo Sapiens' skull altered by the hyper-methylation in the regulatory region of the BAZ1B gene but that this also drastically reduced reactive aggression in anatomically modern humans. To this, humans owe their prosocial behaviour. So we may assume that the development of language ability and cognitive ability went hand in hand. Also that it was complemented by development of empathy, because the mirror neurons, used for this purpose, were available very early on, even in monkeys[17].

Modern humans are **a lot less reactive aggressive** and **more cooperative** than many of our ancestors. And we, too, exhibit a significant physical change: Though our brains are big, our skulls are smaller, and our brow ridges are less pronounced. Neurologists differentiate between reactive aggression and proactive aggression. To be clear, reactive aggression is meant here.

17 Rizzolatti G, Fadiga L, Gallese V, Fogassi L (March 1996). "Premotor cortex and the recognition of motor actions". Brain Research. Cognitive Brain Research. 3 (2): 131–141. doi:10.1016/0926-6410(95)00038-0. PMID 8713554. <https://www.sciencedirect.com/science/article/abs/pii/0926641095000380>.