Are feralization and domestication truly mirror processes?

Amy Niego¹ and Antonio Benítez-Burraco²

1. PhD Program, Faculty of Philology, University of Seville, Seville, Spain

2. Department of Spanish, Linguistics, and Theory of Literature (Linguistics), Faculty of Philology, University of Seville, Seville, Spain

Abstract

Feralization is the process by which a once-domesticated animal returns to a wild-like state due to desocialization from humans. Whether feralization results from a true reversion of the physiological and genetic mechanisms underlying domestication or whether it involves a return to a wild state by other means is still a controversial issue. In this paper we provide a comparative account of both processes. We highlight the physical, behavioral, and neurobiological traits of domesticated animals that appear to be reversible, as well as those others that are resistant to change in cases of feralization. Additionally, we compare the genetic signatures of domestication and feralization, and identify a core set of genes involved in both process that could account for the reversion of selected traits in feralized animals. We conclude with a discussion regarding the ultimate reasons for the differences and overlaps attested between feralization and domestication.

Keywords: feralization; domestication; physical traits; Behavioral traits; Brain; genomic differences

Introduction

Domestication has long been the subject of scientific inquiry; since Darwin's *The Variation of Animals and Plants under Domestication* (1868), differences between domesticated and wild animals have been noted, studied, and debated. Interest in the process of domestication has also grown recently because of claims that the human species may have undergone a process of self-domestication, an idea which also dates back to Darwin's *The Descent of Man, and Selection in Relation to Sex* (1871). The reason is that, when compared with extant primates and extinct hominins, we exhibit many of the traits commonly found in domesticates. These traits are hypothesized to have contributed to the emergence of some of the most distinctive human-specific features, including our advanced social cognition and our sophisticated technology and culture (Hare, 2017), but even, perhaps, the sort of languages we speak (Benítez-Burraco and Progovac, 2020).

Interestingly, an opposite condition to domestication exists, namely, feralization. Feralization can be characterized as the process by which a once-domesticated animal returns to a wild-like state due to desocialization from humans, or the absence of human socializing presence (Daniels and Bekoff, 1989). Whereas domestication mostly results from selection for tameness, feralization mostly involves the reactivation of mechanisms triggering reactive aggression. Human self-domestication (HSD) seemingly started long ago, soon after our inception, but it might have proceeded gradually, with signs of domestication reaching their peak only recently, seemingly at the end of the Upper Paleolithic (Leach 2003; Cieri et al., 2014). In truth, candidate genes for mammal domestication show evidence of positive selection in Europe as recently as 6 kya

(Benítez-Burraco et al., in press), whereas the presentation of self-domestication features in present-day human populations can be also variable (Gleeson and Kushnik, 2018), reinforcing the view that self-domestication is not a totally fixed phenotype in humans, more or less the same as in animal domestication.

Hypotheses regarding the effects of HSD on the evolution of human distinctive features, like culture or language, can only be tested indirectly, mostly through the examination of the effects of selected features brought about by HSD in present-day populations, such as increased teaching and learning, enhanced play behavior, or the sophistication of languages or cultural practices through a cultural mechanism. Nonetheless, we have no access to early stages of HSD, when reactive aggression is hypothesized to have still been common. Interestingly too, cases of feralization in humans have been documented that might potentially enable us to achieve a more confident view of such early stages, but only if human feralization (HF) can be construed as the opposite, mirror condition to HSD. The term ‘feral child’ can be found in the literature and refers to children deprived of human contact, either intentionally or through accidental circumstances. These children exhibit abnormal development or attenuated presentation of many of the traits that are hypothesized to be modelled or enhanced by HSD, from social cognition to language (Stendler et al., 1952; Kapoor, 1973; Fromkin et al., 1974; Lane, 1976; Butler, 2003; Steeves, 2011). Significantly, feral children are typically reported to exhibit increased aggression, which is the opposite hallmark (and the triggering factor) of HSD (Bettelheim, 1959). Certainly, the “feral” phenotype in humans is not easy to define and characterize, mostly because feral features are claimed to have resulted from pre-existing pathological conditions like autism, mental retardation, ‘reactive attachment disorder’, or any number of other developmental disabilities (see Bettelheim,

1959 for discussion). Additionally, in most cases feral features in these children result from extreme isolation, whereas feralized animals still maintain some social contact with conspecifics, as we discuss below. That said, and with all these qualities in mind, feral children could be the most direct approximation to “feral” humans that we have.

In order to use the HF phenotype as a proxy for previous stages in the process of HSD, it is crucial to determine whether feralization involves a true reversion of domestication. Since domestication occurs at various levels (physical, behavioral, genetic, etc.) and to different degrees, it is of interest to see which traits revert when the pressures of domestication slacken due to feralization and which genetic mechanisms are involved. These features could be hypothesized to be the most prone to change under the (self-)domestication forces, but also the most sensitive to environmental differences, and ultimately, the ones that most recently appeared in humans and that are most variable among human groups. It can be further expected that these features result mostly from epigenetic changes that are reversible. Conversely, the traits of domestication that are resistant to change in cases of feralization could be hypothesized to have resulted from fixed changes in gene sequences between feral and domestic animals, and more generally, from the first modern humans to present-day humans.

In summary, the aim of this paper is to explore domestication through the lens of a potentially contrary process: feralization. As noted, this should enable further more confident examinations of HSD through the lens of cases of feral humans and related conditions (and vice versa). The paper is structured as follows. First, we provide a brief overview of the domestication process, with a focus on the so-called ‘domestication syndrome’ (DS). The DS encompasses the set of

shared features purportedly found in all domesticates and resulting from genetic and epigenetic changes in a set of core candidate genes for domestication (see Wilkins et al., 2014 for discussion). The existence of a DS is controversial and this is why we will also review the various ways in which it has been found to manifest in animals. Second, we parallel specific areas of the domesticated phenotype with research on feral animals, highlighting similarities and differences between domestication and feralization. Thirdly, we focus on the genetic underpinnings, with the aim of identifying a core set of candidate genes that contribute to feralization, but also of discussing whether there is some overlap with genes involved in domestication that can account for some unifying mechanism for both process. We conclude with a discussion regarding the ultimate reasons for the differences and overlaps attested between feralization and domestication, as well as regarding the utility of feralization for future studies aimed to provide a better understanding of the effects of HSD.

2. Animal domestication and animal feralization: a (critical) overview

Humans started domesticating animals a long time ago. Dog domestication might have begun as early as 45-40 kya in Europe, with first remains of proto dogs dating from around 30 kya (Germonpré et al., 2009, 2012, 2015; Ovodov et al., 2011; Prassack et al., 2020). Nonetheless, in spite of having been selected for diverse reasons, most domesticated animals share a set of physical, behavioral and even cognitive features that differentiate them from their wild conspecifics. According to Wilkins and colleagues (2014) a DS can be posited that accounts for these shared features, which include smaller brains and altered brain connection and function, smaller teeth and jaws, increased docility, earlier sexual maturation, more frequent estrous cycles,

changes in hairiness and pigmentation, reduced sexual dimorphism, and neoteny. These authors have further hypothesized that the DS comes mainly from the selection against reactive aggression and increased tameness, which is involved in most if not all processes of domestication, and which directly targets the neural crest function (Fitch, 2012; Wilkins et al. 2014). Neural crest cells (NCCs) are a type of stem cell that appear during embryogenesis at the neural crest, the edge of the neural tube. They eventually migrate throughout the body to form the skull and tooth precursors, sympathetic ganglia, adrenal medulla, and other areas of developing vertebrates: all of the tissues that are affected by the DS are derived from the neural crest, or are influenced during their development by the neural crest. More specifically, Wilkins and colleagues hypothesized that the deficit in neural crest derived tissues comes from the inhibition of proliferation of the neural crest cells at the final sites, due to defects in migration. This idea is supported by the fact that the parts of the body which are farther from the neural crest cells' origin (like the face, tail, and limb extremities) are still affected, an indication that neural crest cells are not reaching the distant sites in sufficient numbers. In turn, developmental reduction in NCCs input is hypothesized to be due to changes in preexisting genetic variants that affect NCCs at the final sites.

The theory of a unified DS resulting from reduced input to NCCs, and ultimately of domestication being a mild form of neurocristopathy, is not universally accepted. To begin with, the very idea that a greater degree of aggression correlates with less features of the DS is controversial, and in some cases both types of features appear to be segregated (Hart, 1996). More importantly, the features encompassing the DS present in a variable fashion in domesticated animals. According to Sanchez-Villagra and colleagues (2016) not every domesticated species exhibits all the characteristics of the DS. As pointed out recently by Lord and colleagues in their (2020) critique

of Belyaev and Trut's notorious farm fox experiment (which contributed decisively to the idea of the DS in general), most of the traits purported to be part of the DS do not meet the three criteria for being considered part of the syndrome: i) the trait should appear in conjunction with selection for tameness; ii) the trait should be significantly more popular in the selected population; and iii) the trait in question should be associated with tameness in the individual animal, and not just the population overall. One way of reconciling these apparently disparate positions is to argue that the DS manifests itself differently in different species, with many of the same traits being involved, but with traits being expressed to varying degrees and sometimes not being present at all (see Sanchez-Villagra et al. 2016, Wilkins, 2020, or Zeder, 2020 for further discussion).

From a genetic perspective, one important takeaway is, as noted, that the DS is most likely influenced by multiple networks and alleles, each with a relatively small contribution to the phenotypic result, and with most changes in selected genes being epigenetic by nature (see Wilkins et al., 2014 for a table of core candidate genes). This is in line with advances in the genetics of domestication over the last two decades that have revealed that domestication in many species cannot be traced back to a single event, but most likely occurred at various places and times throughout human history (Bruford et al., 2003, Larson et al., 2005, 2010). For instance, a study by Bruford and colleagues (2003), using mitochondrial DNA to trace lineages of domesticated livestock in the New and Old Worlds, concluded that domestication happened in many parallel and often isolated events. Thus, each domesticated population of livestock had its own genetic markers and traits, and the mixing of DNA lineages over time as populations moved and/or were introduced to other domestic populations made it very difficult to interpret the genetics of domestication in general. Likewise, the famous farm fox experiments (Trut et al. 2004, 2009)

consistently pointed out that domestication is certainly not a linear gradual process but rather something that can happen on a very rapid scale, with multiple alleles, rather than new mutations or accumulations of recessive alleles, being responsible for the changes resulting from selection under domestication. At the same time, when one focuses on a trait-by-trait view of domestication, most differences observed between domesticated and non-domesticated animals result from epigenetic changes. In their research on dogs and wolves, Lindblad-Toh and colleagues (2005) found that the two species are quite similar at the genetic level, with only 0.1% difference of SNPs in their entire genome. In contrast, as found by Sundman and colleagues (2020), dogs and wolves have very distinct profiles of DNA methylation, primarily in the brain. Similar findings have been observed in chickens and their wild counterparts (Nätt et al., 2012), and in guinea pigs, pigs and rabbits, compared to their wild counterparts (Albert et al., 2012).

As noted, feralization is the process of domesticated animals being introduced back into wild-type environments. If domestication is indeed a type of ‘syndrome’ (with all the precautions discussed above) triggered by selection for tameness and social tolerance, presenting in a variable fashion, resulting mostly from physiological changes and brought about by mostly epigenetic changes, then it stands to reason that some traits may be reversible, or at least exist on a sliding scale, provided that the environmental circumstances change towards reduced social contact. A look at feralization through the framework of the DS may thus provide some answers on which traits are truly dependent on specific conditions of domestication (e.g. selection against aggression), and which features have been fixed in domesticates and are thus irreversible. Here one should keep Dollo’s principle in mind: living organisms as a rule do not reverse development based on reversal of the environmental conditions thought to influence their evolution (Dollo, 1893). Feralization, it seems,

should not be an exception. Dollo's principle mostly works for complex characters resulting from the evolutionary accumulation of mutations in many different genes (it is unlikely that all they can simultaneously reverse--see Collin and Miglietta, 2008 for discussion). Nonetheless, true reversions can emerge if ancestral developmental programs are preserved (but silenced) in the derived populations (see Cabej, 2012 for discussion). In this case, reversions to the wild-type phenotype can be facilitated by the fact that, as noted, most differences observed between domesticated and non-domesticated animals result from epigenetic changes. As we discuss in more depth in section 4 below, research on the genetic basis of feralization (as rare as it may be) points to the fact that the genes selected when domesticated animals go feral are different from the genes selected when wild animals were domesticated, although some interesting overlaps exist too.

It is also important to address another common misconception: that domesticated animals are ill-equipped to survive life in the wild compared to their wild counterparts (incidentally, from this perspective, one could expect that any genetic profiles of domestication would be 'weeded out' over time in feral populations as a result of natural selection). While this may be true in some instances, there are also many cases where domesticated traits have been shown to be advantageous in feral populations (e.g. Pan et al., 2018, Gering et al., 2019). Thus, as far as feralization is concerned, it's not a question of domesticated traits and genes merely reverting to the wild state when animals go feral. Instead, the fitness associated with the domesticated or the wild trait, allele, or regulatory network, will be always dependent on the specific feral environment and population.

In the subsequent section of the article, we compare observed feral and domestic traits, highlighting similarities and differences, whereas in section 4 we explore possible underlying

connections at the genetic level when the research exists to do so. There is a large body of research dedicated to defining and characterizing morphological, behavioral, and even cognitive traits of domestication, as well as its genetic underpinnings, but similar research on feral animals is much more scarce. Although we will consider research on various types of feral and domesticated organisms, a great deal of discussion will be dedicated to the Australian dingo. This is because the dingo, unlike many other feral animals, has been isolated for over 8,000 years with minimal intervention from other wild or domesticated dogs due to its remote habitat (Zhang et al., 2020). In contrast, research on feralized livestock, pigs, or chickens is more difficult to interpret because of the frequent mixing of DNA lineages and interaction with both wild and domesticated counterparts.

3. Domestication and feralization: the phenotype

In this section, we explore possible connections and divergences between domesticated and feral animals. We first focus on body traits. A subsequent subsection does the same with behavior, and a final subsection is dedicated to what is known of the feral and domesticated brain. Our findings are summarized in the Figure 1. Genetic or epigenetic rationales for these features areas are highlighted in section 4 below.

Figure 1. A graphical summary of the similarities between wild, feralized, and domesticated animals. The companion images were retrieved from Unsplash (<https://unsplash.com/>) and Wikipedia (<https://en.wikipedia.org/>), which provide freely-usable images.

Body traits

Shorter snouts

One of the most commonly cited traits of domestication is the general shortening of the nose/snout, which is observed in dogs, mice, cats, foxes, pigs, sheep, goats, and cattle (Trut, 2009; Zeder, 2012; Wilkins et al. 2014). From the perspective of the DS, this shortening is attributed to lower input numbers in NCCs (Etchevers et al. 1999; Creuzet et al. 2004). There is conflicting research as to whether or not this trait is retained in feral animals. Observations of the feral hogs found in the American south show that, even after many generations of living in the wild, their smaller snouts still set them apart from their wild counterparts (Physical Characteristics of Feral Hogs, 2019). By contrast, a comprehensive study by Kruska and Röhrs (1974) on pigs from the Galapagos Islands and Europe found that feral pigs exhibit significantly longer snouts than those of their domestic counterparts, perhaps due in part to relaxation of certain selective pressures. In a similar vein, Bach (2007) reports that, in the absence of domestication pressures, pigs will quickly revert to a wilder phenotype, exhibiting, specifically, features such as longer snouts in a matter of generations. As noted, the dingo has proven to be a valuable research subject with much to contribute here. Various studies (e.g. Smith et al., 2018; Ballard and Wilson, 2019) found that dingoes do exhibit shorter snouts than wolves, although the variation of nose length in domesticated dogs makes it hard to compare on that front.

Dentition

Changes in tooth size and morphology have also been highlighted by many studies addressing the differences between domesticated animals and their wild counterparts (see Belyaev, 1974; Wilkins et al., 2014). Again, this trend is seemingly in keeping with the theory of the central role of the

neural crest in domestication, since NCCs play a direct role in tooth development (Hall 1999; Le Douarin and Kalcheim 1999; Gilbert 2003). In research on feral pigs, Evin and colleagues (2015) found evidence that feral populations of pigs on the Italian islands of Corsica and Sardinia had smaller teeth than any of the wild or domesticated groups they were compared to. Interestingly, the shape of their teeth was more similar to wild boar than domesticated pigs in the area. These authors hypothesize that feralization might have caused the teeth to revert back to a more wild-type morphology due to relaxed selection in their environment, although one cannot discard that wild boars have contributed in some way to the gene pool, influencing the shape of the teeth through admixture. In canids, research on dingoes and dogs has shown that the former exhibit larger carnassial teeth and longer canine teeth (Smith and Litchfield, 2010), which seems to point to a reversion towards wild type morphology in the case of dentition.

Ear morphology

Another trait commonly found in domesticates is floppy ears, particularly in dogs, rabbits, foxes, and livestock (Wilkins et al., 2014; see specifically Webster et al., 2015 for genetic determinants of floppy ears in dogs). Interestingly, research on dingoes and their domestic counterparts, kelpies, suggests that ear morphology (floppy vs. upright ears) is a trait that can revert when animals go feral (Chew et al., 2019).

Pigmentation

Domestic animals commonly display coloration that sets them apart from their wild counterparts. The typical piebald (black and white spotted) coloration is among the most widespread, and is often seen in domesticated cows, goats, horses, and pigs (Wilkins et al, 2014). In the widely-cited

farm fox experiment, Belyaev found that sometimes it was just a question of one or two generations before the piebald coloration appeared in foxes selected for tameness (Trut, 1999). As of yet, studies on coloration in feral animals have not yielded a clear picture of whether or not domesticated phenotypes for coloration revert when they undergo feralization. It seems instead that some domesticated traits are preserved if they confer some adaptive advantage in the new, wild type environment. Hence, in feral pigs, a great deal of variation in coat color has been found (Gering et al., 2019), with some dominant coat colors having a domestic origin (Linderholm et al., 2016). Likewise, in feral sheep, a lighter coat color with a domestic origin has undergone positive selection due to the fact that it increased overall fitness (Feulner et al., 2013). Domestic features can be eventually transferred to wild conspecifics. Accordingly, a darker coat color, associated with domesticated dogs, now prevails in some wolves, as it likely enhances survival (Anderson et al., 2009). The same trend can be observed in more distant species, like feral pigeons, that have retained the wide variation in coloration originally coming from artificially selected coloration during pigeon domestication, as each coloration type has proven to be advantageous to specific environments (Roulin, 2004; Derelle et al., 2013).

Additional features

In dingoes, another interesting morphological trait is the absence of dew claws. Dew claws are vestigial toes on the hind legs, which are common in many domesticated breeds, large and small (Jackson et al., 2017). In contrast, wild canids such as wolves do not have dew claws, and neither do dingoes (Jackson et al., 2017).

Behavioral traits

Behavior is perhaps the most noticeable aspect of domesticated animals, and, according to a great deal of research, the source of domestication in the first place, since domestication first and foremost demands selection for tameness. It is also the most reliable indicator of whether or not an animal is truly domestic; while it is possible for a domestic animal to appear wild on the surface, it is much less common for domesticated animals to display wild behavior, especially when it comes to approach behavior and familiarity towards humans. We focus on three salient behavioral aspects: tameness (including aggression/familiarity towards humans), predator and stress response, and hunting behavior. However, we also provide some hints about sexual behavior, which is also affected by domestication in some significant ways.

Tameness

In truth, ‘tameness’ is a vague term, and usually refers to the prosocial behavior of an animal towards conspecifics as well as familiarity and approach behavior towards humans. Most research indicates that this tameness does indeed recede when human contact is removed; for example, a study by Rose and colleagues (1985) found that in general, feral roosters showed higher levels of aggressive behavior when compared to domestic roosters. Similar trends have been found in feral vs. domestic cats in terms of approachability to humans: feral cats are much less likely to approach humans, displaying a seemingly deep-seated fear/cautiousness which cannot be overcome with mere contact (Owens et. al., 2017). Returning to the oft-cited dingo, Johnston and colleagues (2017) examined behavior in dingoes kept as pets, finding that, although dingoes do initiate eye contact with humans (unlike wolves), they hold it for a shorter time than domesticated dogs, indicating that dingoes fall somewhere in the middle of the wild- domestic sliding scale in this respect. Interestingly, Kaminski and colleagues (2019) found that domesticated canids possess an

extra muscle that gives them more ability to interact with humans via gaze, but that dingoes (and wolves) lack it.

Further investigation has also revealed some differences in vocalization behavior between domesticated and feralized animals. Smith and Litchfield (2010) pointed out that, like wolves, dingoes howl much more than they bark, while domesticated dogs tend to bark and vocalize much more, perhaps as a result of proximity with humans. Tavernier and colleagues (2020) found similar results for feral cats: their vocalizations are different, and in general they vocalize much less than domestic cats do. In this way, feral animals share more with their wild counterparts than domesticates. Seen from this angle, there seems to be at least the appearance of a reverse process at work, with feralization being a return to wild type behavior.

Predator/stress response

Another prominent trait in domesticated animals is decreased response to predators (Price, 1984). This can be attributed to a difference in basal cortisol levels and hypothalamic-pituitary-adrenal (HPA) axis reactivity, among other factors (see Trut et al., 2009; Kaiser et al., 2015 for discussion). Reduced activity of the HPA axis affects the glucocorticoid production by the adrenal glands, as well as the basal levels of adrenocorticotrophic hormone in plasma, and more generally, the adrenal response to stress (Naumenko and Belyaev, 1980; Oskina, 1996).

Research on predator response in feral animals is scarce. One study about guppies reintroduced to a wild environment suggests that feral animals might have some heightened defense responses to predators when compared to their domestic counterparts: specifically, feralized guppies practiced

shoaling, i.e. swimming in a group, much more than domesticated guppies, both at a baseline and when faced with predators (Swaney et al., 2015). At the same time, in a study of feral dogs in Italy, Boitani and Ciucci (1995) found that feral dogs, despite their wilder environment, still seemed to retain lower levels of observational capacity and lower responsiveness to environmental threats.

Hunting behavior

There is a host of anecdotal evidence that feral animals are less adept at hunting than wild ones, and in general this idea is supported by research. Studies by Corbett (1979), Gil-Sánchez and colleagues (1999), and Biro and colleagues (2005), all point to the fact that feral and domesticated cats both tend to hunt prey that requires less skill to catch, like ground-dwelling rodents, while wild cats focus on tree-dwelling or larger terrestrial prey that requires much more hunting skill to capture. In their study of dogs and wolves, Boitani and Cuicci (1995) found that feral dogs generally fall in the domesticated category when it comes to hunting: their diet consists of easy to catch animals, and even after many years in the wild, they are still dependent on humans to survive, regardless of the fact that they have little to no contact with humans. Contrasting conclusions have been made in studies on dingoes, however. Fleming and colleagues (2001) report that dingoes hunt using the same tactics as wolves do to stalk and kill large prey like cattle, water buffalos, and wild horses. Since the dingo is the product of over 8,000 years of feralization, it could be argued that hunting behavior is a reversible trait, but it takes time to revert to the wild condition.

Reproduction and fertility

A last behavioral feature that is consistently prevalent in domesticated animals is increased fecundity (Setchell, 1992; Wilkins et. al., 2014). Studies on feral pigs and chickens indicate that

increased rates of reproduction and estrous cycles continue from domestic populations to feral ones, proving to be quite beneficial, as one would imagine (Gethoffer et al., 2007; Johnsson et al. 2016). Nonetheless, this increased fecundity in feral populations may be the result of admixture with domestic populations, as shown in the case of the feral pig populations, whose rate of reproductive success are higher for those living near domestic pigs (Gering et al., 2019). True feralization in absence of contacts with domesticated animals may revert reproduction and fertility patterns to the wild state. Thus, dingoes, which live in an isolated environment with little opportunity for admixture, have less frequent estrous cycles, showing more similarity to wolves than they do to dogs in this respect (Lord et al., 2013; Ballard and Wilson, 2019).

Another element of fertility in feral animals that seems to suggest reversion to the wild is that of delayed sexual maturity when compared to domestic animals. In their study of 6 members of the canid group which included domesticated dogs, wolves, jackals, and dingoes, Lord and colleagues (2013) found that, in general, feral dogs such as the dingo began to breed at a later age than their domestic counterparts. These authors attributed this in part to factors such as distribution of resources, as well as the fact that feral dogs have less frequent estrous cycles (Lord et al., 2013). Pan and colleagues (2018) also found evidence that certain domesticated traits which relate to reproductive success, such as horn size and shape in feral sheep, are retained in feral populations due to the sexual fitness these traits provide (Pan et al 2018).

The feral brain

Reasons for many of the differences reviewed above between domesticated and feral animals, particularly those impacting behavior, boil down to the brain. This is why in this last subsection

we discuss what the research can contribute to our understanding of the feral vs. the domestic brain.

Brain size and organization

A reduction in brain size is one well-documented feature of domestication, although this reduction is by no means uniform across species or even within the brain itself (see Kruska, 2005, Trut and Kharlamova, 2009, or Wilkins et al., 2014 for discussion). Kruska (1988, 2005) points out that the larger the brain to begin with, the greater degree of reduction in domestication. This has been found to hold true with pigs, (33% reduction in domesticates), dogs (30% smaller than wolves), herbivores (14-24% reduction) and rodents (minimal reduction), as well as birds (Ebinger and Röhrs, 1995; Zeder et al., 2012) and fish (Marchetti and Nevitt, 2003). At the same time, as noted, the reduction of the brain is not uniform, impacting more on the forebrain and accompanying structures, which are phylogenetically younger (Kruska, 2005; Wilkins et al., 2014). The forebrain does not only contain areas devoted to movement and sensory integration, but also to “higher order” functions, such as reasoning, communication, or expression of emotions. In many cases, motor areas become more reduced, whereas visual and/or integration areas are less affected or even enhanced in domesticates. Hence, olfactory and auditory function in the pig brain are less reduced by domestication than visual structures or motor functions (Plogmann and Kruska, 1990); rats and mink exhibit a significant reduction in motor functions, but lesser reductions in visual and olfactory regions (Kruska 1988, 1996); and memory and learning areas of the brain in homing pigeons show a distinct increase under domestication (Rehkämper et al., 2008). Perhaps more importantly, the limbic system, which supports many aspects of emotion, is altered in a variety of domesticates, seemingly contributing to the attested changes in tameness and docility (Kruska,

1988). More specifically, compared to chimpanzees, bonobos (thought to have gone through a self-domestication process) exhibit a larger amygdala, particularly in the dorsal area, with a larger pathway to the ventral anterior cingulate cortex (vACC) (Rilling et al., 2012). This amygdala/vACC pathway has been implicated in inhibition of aggression (Davidson et al., 2000; Meyer-Lindenberg et al., 2006; Blair, 2008), which is central to the behavioral phenotype of domesticates. Moreover, in studies on the hippocampus of domesticates, Kruska (1988, 2005) found that domesticated rats, pigs, sheep, dogs, and llamas all showed significant reduction in their hippocampus, leading to potential functional differences, which seemed to become more exaggerated in more domesticated forms (poodles, pigs, and sheep showed a reduction of over 40%). That said, other studies suggest that domestication can result in an enlargement of the hippocampus (Rehkämper et al., 2008; Huang et al., 2015; Welniak-Kaminska et al., 2019). Recent studies (Huang et al., 2015) indicate that domestication may actually be responsible for neurogenesis in the hippocampus of adult foxes.

There is still much to be studied and learned about the effects of feralization on the brain. Studies that have focused on brain size on the whole do not support the idea that the effects of domestication can be somehow undone through feralization (Kruska and Röhrs, 1974; Birks and Kitchener, 1999; Röhrs and Ebinger, 1999), even in the case of animals that have been feral for thousands of years, like Mediterranean sheep (Groves, 1989). Once again, dingoes may prove to be an exception here. While Shultz (1969) found the brain size of dingoes to be more within range of other domestic dogs when compared to wolves, other more recent studies have found contrasting information. For example, Smith and colleagues (2018) found that dingoes have a larger and more encephalized brain than domestic dogs do, suggesting that perhaps thousands of years of

feralization may indeed have affected their brains and caused them to revert back to a pre-domesticated size. This gives some support for the idea that, at least in some ecological environments and/or for some species, brain size could be one domestication trait that is reversible through feralization.

Aside from brain size, structural differences between the feral and the domesticated brain can be found. Kruska and Röhrs (1974) studied Galapagos pigs, a type of feral pig that have been living in wild conditions for up to 140 years on some of the islands, and compared them to European domestic pigs. Although the sample size was small, they found that feral pigs had a larger medulla oblongata than the domestic pigs, as well as a smaller cerebellum, that could be linked to changes in motor behavior. Another interesting finding was the enlargement of the allocortex in feralized animals, which, as noted above, houses the olfactory and limbic systems, and is implicated in domestication. The olfactory system (or certain portions of it) is found to be enlarged in feral animals compared to domesticates, as in feral pigs, which exhibit an olfactory bulb about 28% larger than the domesticated pigs, making that area in the feral brain more similar to European wild boars than domesticated pigs (Kruska and Röhrs, 1974). Regarding the limbic system, the hippocampus and the nuclei basalis have been both found to be around 25% larger in feral pigs than in domestic pigs (Kruska and Röhrs, 1974), which seems to support the idea that the hippocampus might undergo a partial 'return' to more wild-type sizes as a result of feralization.

4. Domestication and feralization: the genotype

As noted in the second section, there is an ever-growing number of genes that are thought to be implicated in the process of domestication (see Wilkins et al., 2014 for a core set, see Niego and Benitez-Burraco, 2019 for a recent, expanded list, which can be found in Supplementary file 1; column A). Key concepts to keep in mind are that, as Jensen (2006) or Wilkins and colleagues (2014) point out, domestication is most likely caused by mutations or epimutations in regulatory genes or dosage- sensitive genes which in turn impact a network of linked genes, but also that the multiple changes associated with domestication arise to a great extent from pre-existing genetic variation. Overall, this allows for significant phenotypic changes without big allelic differences between wild and domesticated animals. This concept holds true for feralization as well. From a genetic perspective, feralization poses more of a challenge, since usually it is very difficult to know whether genetic differences found within a feral population are due to feralization per se, or crossbreeding with wild populations (see Zhang et al., 2020 for discussion). The most comprehensive study to date about the genetics of feralization was conducted by Zhang and colleagues with dingoes, which, as noted, have remained isolated from both wolves and dogs for thousands of years. This enabled the authors to find around 50 genes that have been selected in dingoes and that emerge as robust candidates for feralization, with a small number of them having been selected in dogs too, although perhaps only in certain breeds. This means that the same genes can be indeed involved in both domestication and feralization, giving some support to the view that feralization involves a sort of reversion also at a genetic level. Still, many others of the candidates highlighted by Zhang and colleagues have not been yet related to domestication.

In order to achieve a more comprehensive understanding of the genetics of feralization and its connections with the genetics of domestication, we have compiled an improved list of candidates

for feralization (Supplementary file 1; column A). For this, we merged Zhang et al.'s candidates with other ones resulting from other studies about feralization, specifically, Pan et al.'s (2018) and Gering et al.'s (2019). We then performed Gene Ontology (GO) analyses to know whether these genes play roles at the molecular and cellular levels, and/or map to biological processes, regulatory pathways, cell types, or aspects of body development and function, of interest for the process of feralization, as we have characterized it in the previous section. Functional enrichment analyses were performed with Enrichr (<https://maayanlab.cloud/Enrichr/>; Chen et al., 2013; Kuleshov et al., 2016). We considered biological processes, molecular functions, and cellular components with associated p-values < 0.05 as enriched. We found that candidates for feralization are significantly related to hormone homeostasis, particularly, androgen, steroid, and thyroid hormone homeostasis (GO:0050681, GO:0030521, GO:0035258, GO:0046966, GO:0051427), but also to gene regulation (GO:0001133, GO:0001085), cell differentiation (GO:0003309, GO:0030219, GO:0045606), muscle tissue development (GO:0048745, GO:0060537, GO:0010763), and brain development (GO:2000178), which are all aspects affected by feralization (see Supplementary File 2 for details). We also searched the literature (via PubMed <https://pubmed.ncbi.nlm.nih.gov/> and GeneCards <https://www.genecards.org/>) to know more about the precise roles played by these genes, with a focus on the features involved in feralization, as discussed in the previous section (see Supplementary File 3 for details). Because we were particularly interested in disentangling the shared genetic basis of feralization and domestication, we then compared our list of candidates for feralization with our previous list of candidates for mammal domestication, which encompasses 764 candidate genes for mammal domestication (Supplementary file 1; column B). This list resulted from merging genes that have been found positively selected in several mammal domesticates: Guinea pig, pig, rat, dog, cat, cattle, domesticated fox, horse, rabbit, and sheep

(Womack et al., 2005; Trut et al., 2009; Albert et al., 2011; Axelsson et al., 2013; Bellone et al., 2013; Carneiro et al., 2014; Montague et al., 2014; Qanbari et al., 2014; Schubert et al., 2014; Wilkins et al., 2014; Wright et al., 2015; Cagan and Blass, 2016; Freedman et al., 2016; Zapata et al., 2016; Benítez-Burraco et al., 2017; Theofanopoulou et al., 2017; Pendleton et al., 2018). This comparison enabled us to obtain a set of 15 genes involved in both feralization and domestication (Supplementary file 1, column C), to which we added the 13 genes highlighted by Zhang and colleagues (2020) as common to both processes (Supplementary file 1, column D). After removing the duplicated genes (1), we compiled an improved list of candidates for both feralization and domestication, that encompasses 27 genes (Supplementary table 1; column E). We expected that these genes map to biological processes that are reversed in the process of feralization. To check this possibility, we conducted GO analyses via Enrichr using a significance threshold of < 0.05 . We found that these genes are mostly involved in the differentiation of specific cell types, including melanocytes (GO:0030318), epithelial cells (GO:0003337), eye components (GO:0048596, GO:0031076), parts of the digestive tract (GO:0048565) or cardiac muscle cells (GO:0055026), in many cases through an effect on microtubule assembly (GO:0051415, GO:0051011, GO:0043015) (see Supplementary file 4 for details). We also conducted an exhaustive search of the literature via PubMed in order to achieve a better understanding of the functional roles played by these genes (summarized in Table 1). These genes emerge as promising candidates for accounting for the reversion of domestication traits in feralized animals and accordingly, of features of domestication that can be more sensitive to environmental effects.

Gene name	Protein function	Relationship to domestication/feralization	References

<i>ANKRD28</i>	<ul style="list-style-type: none"> • cell migration • regulation of the DOCK180-Rac1 pathway 	<ul style="list-style-type: none"> • a candidate for both feralization and domestication in canids 	Tachibana et al., 2009 Zhang et al., 2020
<i>ARGHEF7</i>	<ul style="list-style-type: none"> • a putative activator of the Ras-like family of Rho proteins • formation of neural spine and synapses in hippocampal neurons 	<ul style="list-style-type: none"> • implicated in both domestication and feralization of canids 	Bagrodia et al., 1998 Saneyoshi et al., 2008 Zhang et al., 2020.
<i>ENSCAFG00000000697</i>	<ul style="list-style-type: none"> • intercellular signalling 	<ul style="list-style-type: none"> • shows shifted allele frequencies in dogs but not wolves, being thus associated with both domestication and feralization 	Mi et al., 2019 Zhang et al., 2020
<i>ENSCAFG000000003879</i>	<ul style="list-style-type: none"> • serine-type endopeptidase activity 	<ul style="list-style-type: none"> • show shifted allele frequencies in dogs but not wolves, thus being associated with both domestication and feralization 	Mi et al, 2019 Zhang et al., 2020
<i>ERBB4</i>	<ul style="list-style-type: none"> • a receptor of the neuroregulin NRG1 controlling the migration of GABAergic interneurons • plays a key role in synchronizing neural oscillations in the cortex • related to intellectual disability and speech delay 	<ul style="list-style-type: none"> • found among candidate genes for feralization in studies of feral sheep • Nrg1(+/-) mice exhibit decreased social activity 	Sakakibara and Horwitz, 2006 Ehrlichman et al., 2009. Kircher et al. 2009 Veikkolainen et al., 2011 Li et al. 2012 Kasnauskiene et al. 2013 Selçuk et al., 2013 Hou et al. 2014 Benitez-Burraco and Boeckx, 2015 Rolstad et al. 2015

	<ul style="list-style-type: none"> • related to a language-ready-brain core set of candidates • development of striated muscle tissue and the olfactory system 		Pan et al., 2018
<i>KIT</i>	<ul style="list-style-type: none"> • a tyrosine kinase involved in cell proliferation, differentiation, migration and apoptosis • plays a role in stem cell maintenance, gametogenesis, and melanogenesis • contributes to hippocampal synaptic potentiation and spatial learning and memory 	<ul style="list-style-type: none"> • related to piebald coloration • related to feralization in sheep • related to domestication in various mammals 	Katafuchi et al., 2000 Rothschild et al., 2003 Kilsby et al., 2013 Wilkins et al., 2014 Pan et al., 2020 Zhu et al., 2020
<i>MC1R</i>	<ul style="list-style-type: none"> • pigmentation in skin, hair, and eyes 	<ul style="list-style-type: none"> • domestic alleles have been selected in in feral pigs • a candidate gene for feralization 	Gering et al., 2019 Guida et al., 2019
<i>MITF</i>	<ul style="list-style-type: none"> • pigment cell specific transcription of the melanogenesis enzyme genes • development and function of the neural crest 	<ul style="list-style-type: none"> • related to neurocristopathies such as Waardenburg syndrome type 2A (OMIM #193510) • a candidate for feralization in sheep • a core candidate for domestication 	Wilkins et al., 2014 Goding and Arnheiter, 2019 Pan et al., 2019
<i>MSRB3</i>	<ul style="list-style-type: none"> • protein repair and protein metabolism • auditory function 	<ul style="list-style-type: none"> • a candidate for feralization in sheep 	Hibar et al., 2017 Cao et al., 2018 Pan et al., 2018

	<ul style="list-style-type: none"> • regulation of hippocampal volumes in the dentate gyrus and fissure 		
<i>PANX2</i>	<ul style="list-style-type: none"> • formation of the structural component of gap junctions. • expressed in diverse neuronal populations • hippocampal neurogenesis • exploration, sensorimotor symmetry, and anxiety in mice 	<ul style="list-style-type: none"> • related to oculodentodigital dysplasia (OMIM #164200), a condition featuring some traits related to domestication (e.g. orofacial anomalies, small head size) • implicated in behavioral differences in feralization • involved in both feralization and domestication 	Plotkin et al., 2016 Litvin et al., 2006 Swayne et al., 2010 Bargiotas et al., 2012 Zhang et al., 2020
<i>PCSK5</i>	<ul style="list-style-type: none"> • protein and peptide precursors trafficking 	<ul style="list-style-type: none"> • among gene candidates for feralization in sheep 	Choi and Korstanje, 2013 Pan et al., 2020
<i>PRSS37</i>	<ul style="list-style-type: none"> • sperm migration and binding to zona-intact eggs. 	<ul style="list-style-type: none"> • candidate gene for both feralization and domestication in dingoes 	Shen et al., 2013 Zhang et al., 2020
<i>RF00026</i>	<ul style="list-style-type: none"> • mRNA splicing and RNA transport pathways 	<ul style="list-style-type: none"> • correlated to various behavioral traits in different dog breeds (e.g. nonsocial fear, owner and stranger aggression, and aggression towards other dogs) • implicated in both feralization and domestication in 	MacLean et al., 2019 Zhang et al., 2020

		studies on canids	
<i>ROBO1</i>	<ul style="list-style-type: none"> • axon guidance (specifically, thalamocortical axon development in the forebrain) • regulation of neuronal precursor migration • olfactory system function and food seeking • interaural interaction in auditory pathways • vocalization in songbirds • externalization of language as part of the ROBO regulatory network • candidate for dyslexia, and other language disorders and language evolution 	<ul style="list-style-type: none"> • candidate for feralization from studies of selective sweeps in sheep 	<p>Andrews et al., 2006</p> <p>Lopez Bendito et al., 2007</p> <p>Lamminmäki et al., 2012</p> <p>Boeckx and Benitez-Burraco, 2014</p> <p>Wang et al., 2015</p> <p>Benitez-Burraco and Boeckx., 2015</p> <p>Benitez Burraco et al. 2018</p> <p>Pan et al., 2018</p>
<i>RXFP2</i>	<ul style="list-style-type: none"> • regulation of reproduction, cardiovascular function, and neuronal signaling 	<ul style="list-style-type: none"> • linked to increased fitness in feral sheep populations. • candidate for both feralization and domestication 	<p>Scott et al., 2012</p> <p>Pan et al, 2018</p> <p>Gering et al., 2019</p>
<i>S100A12</i>	<ul style="list-style-type: none"> • regulation of cellular function 	<ul style="list-style-type: none"> • candidate for feralization of sheep 	<p>Pietzsch and Hoppmann, 2009</p> <p>Pan et al., 2018</p>
<i>SELENOO</i>	<ul style="list-style-type: none"> • redox control in the mitochondria 	<ul style="list-style-type: none"> • candidate for both feralization and 	<p>Han et al., 2014</p> <p>Zhang et al., 2020</p>

		domestication of canids	
<i>SLC5A1</i>	<ul style="list-style-type: none"> • a sodium-dependent glucose transporter involved in dietary glucose and galactose uptake 	<ul style="list-style-type: none"> • related to dog domestication and feralization 	Axelsson et al., 2013 Li et al., 2017 Zhang et al., 2020
<i>SMO</i>	<ul style="list-style-type: none"> • signal transduction • development of striated muscle tissue • mutations in the gene result in brain, heart, and skeleton anomalies 	<ul style="list-style-type: none"> • a candidate for semi feralization of the sheep 	Pan et al., 2018 Le et al., 2020
<i>SOX6</i>	<ul style="list-style-type: none"> • transcriptional regulation of genes involved in neurogenesis and skeletogenesis • initial neural crest cell differentiation as part of Wnt signalling pathway 	<ul style="list-style-type: none"> • linked to feralization in sheep • differentially expressed in the frontal cortex of certain domesticated animals (dogs, pigs, rabbits, guinea pigs) 	Stellos et al., 2010 Albert et al., 2012 Ebrahimi-Fakhari et al., 2015 Pan et al., 2018 Wang et al., 2018 Tolchin et al., 2020
<i>TAS2R5</i>	<ul style="list-style-type: none"> • reception of bitter taste 	<ul style="list-style-type: none"> • involved in canid domestication and feralization 	Chandrashekar et al., 2006 Cagan et al., 2016 Zhang et al., 2020

<i>TH</i>	<ul style="list-style-type: none"> • conversion of tyrosine to dopamine • regulation of the physiology of adrenergic neurons, and ultimately, of animal behavior 	<ul style="list-style-type: none"> • linked to temperament and behavior in the cattle 	Lourencou-Jaramillo et al., 2012
<i>TRABD</i>	<ul style="list-style-type: none"> • expressed most prominently in the bone marrow • linked to various types of deafness 	<ul style="list-style-type: none"> • linked to both feralization and domestication of canids 	Zhang et al., 2020
<i>TRHDE</i>	<ul style="list-style-type: none"> • inactivation of the neuropeptide thyrotropin-releasing hormone 	<ul style="list-style-type: none"> • under selection in both feralization and domestication • related to the HPA axis, which has implications in the behavior of domesticated and feral animals 	Schauder et al., 1994 Nillni et al., 1999 Zhang et al., 2020
<i>TUBGCP6</i>	<ul style="list-style-type: none"> • part of a large complex in charge of microtubule nucleation at the centrosome 	<ul style="list-style-type: none"> • under selection in both feralization and domestication • associated with Chorioretinopathy-Microcephaly Syndrome (MCCRP; OMIM #251270), which is characterized by several traits found in some domesticated animals (e.g. microcephaly, growth 	Puffenberger et al., 2012 Zhang et al., 2020

		retardation with dwarfism)	
<i>TYRP1</i>	<ul style="list-style-type: none"> • a component of the melanin biosynthetic pathway 	<ul style="list-style-type: none"> • a candidate for feralization (but not domestication), being linked to coat color of feral sheep 	Xu et al., 2013 Gering et al., 2019
<i>ZNF516</i>	<ul style="list-style-type: none"> • transcriptional repression of genes involved in cell proliferation, differentiation, and apoptosis 	<ul style="list-style-type: none"> • related to dog domestication • a candidate for feralization (but not domestication) 	Li et al., 2017 Axelsson et al., 2013 Cagan and Blass, 2016 Zhang et al., 2020

Table 1. Functional characterization of core candidates for animal feralization and domestication.

5. Discussion and conclusions

It is clear from the research reviewed in our paper that both domestication and feralization are complex and dynamic processes. Like many other biological processes and traits, feralization obeys Dollo's law to some extent: once domestication takes place, there is no direct way to reverse the process. Accordingly, not all features of domestication are found reversed in feralized animals. Likewise, only a subset of candidates for domestication are also involved in the emergence of features of feralization. That said, we have highlighted overlaps as well that are worth exploring in more detail. In some cases, discrepancies between domesticates and feralized animals can be explained by specific adaptations of the latter to the new conditions and/or environments imposed by feralization (e.g. changes of diet in dingoes). However, certain distinctive traits of domestication (e.g. management of aggression) can be indeed reversed under feralization, as feralization imposes selective pressures similar to the pressures experienced by wild animals. At

the same time, this reversion of specific features is sometimes achieved via the modification of the same genes that account for the domesticated features, but in other cases this is achieved through alternative routes to those of domestication, seemingly exploiting the available, underlying genetic variation. In this sense, feralization works like domestication. The genes mentioned in this paper as common candidates for domestication and feralization may provide a direction for some interesting future research, as they seemingly point to aspects of domestication that are more sensitive to environmental factors and thus, more adaptive to environmental change.

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