Success of manipulation of genetic architecture to reveal fitness relationships depends on selection history and genetic architecture

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Introduction

Ketola, Boratyński, and Kotiaho’s paper “Manipulating genetic architecture to reveal fitness relationships” (Ketola et al., 2013) advocates the use of experimental inbreeding as a way of determining which traits are important to fitness. Measuring fitness is tricky and most data on the importance of various traits to fitness is correlational. The authors therefore suggest that it’s better to try to manipulate the genetic architecture via inbreeding, and then measure the effect of inbreeding on the trait(s) of interest. Traits that are under directional selection should show directional dominance; that is, that recessive alleles should preferentially be deleterious. This is because any favourable recessive mutations will quickly go to fixation, and any deleterious dominant mutations will quickly be purged. Inbreeding exposes these deleterious recessives, resulting in a change in the trait mean in the opposite direction to that of ongoing selection. From this we can draw conclusions about which traits are related to fitness, and in what way.

Merits

The point that more experimental manipulations are needed when measuring how various traits contribute to fitness is a very pertinent one. In their paper Ketola et al. particularly focus on basal metabolic rate, but the same is true of other questions in life history theory, where there is a classical problem in demonstrating trade-offs between fitness components. It seems obvious that an organism should be limited in the resources it can allocate to various processes, such that there should be a trade-off between e.g. fecundity and lifespan. However in natural populations it can be hard to find evidence of such patterns, probably because individuals vary so much in overall condition that the trade-off is obscured. In such cases, correlational evidence is not enough—only an experimental manipulation can reveal whether there truly is a trade-off or not. The same is true of the contribution of various traits to fitness. A correlative study may show that traits X, Y, and Z contribute to fitness. However many traits are genetically and phenotypically correlated within an individual, so if X, Y, and Z are correlated with each other, we can’t be sure which traits are really driving the relationship with fitness without doing an experimental manipulation. There are of course statistical methods to try to deal with this problem, but this is a suboptimal solution at best. The method advocated by Ketola et al. is particularly useful since it involves manipulating fitness itself, rather than manipulation of the traits in question.

Critique

That being said, the method has some limitations. The success of the inbreeding approach depends on the type of selection the trait has undergone, and the demographic history of the population in
question. For directional dominance to evolve, a trait must have been subject to directional selection rather than stabilizing or divergent selection. One must presume that this pattern of directional selection will have to be reasonably stable over time as well, at least on ecological timescales, in order for deleterious recessive mutations to have accumulated. In addition, these deleterious recessive alleles may already be purged in populations that have experienced elevated levels of natural inbreeding, leaving no signature of directional dominance. However Ketola et al. acknowledge these limitations in their paper.

Discussion

Experimental inbreeding as a manipulation of fitness has previously been successfully applied to studies of sexually selected traits (see Ketola et al. for references). However as I mention above, a trait under stabilizing selection will not be subject to directional dominance, but may still be important for fitness. In this case we will not see a change in the trait mean, which could lead us to wrongly conclude that the trait is not important to fitness. The success of this approach in a sexual selection context does not imply that it will be equally successful for other types of traits, because sexually selected traits are generally expected to often be subject to chronic directional selection. For example, lifetime reproductive success in Drosophila has been demonstrated to be maximized at an intermediate egg lay rate, since this trait trades off with longevity (Pum Lee et al., 2008). This will result in stabilizing selection on egg lay rate. Yet I don’t think one can reasonably claim that this trait is not closely related to fitness. Basal metabolic rate, the main trait under discussion in Ketola et al.’s paper, could easily be subject to stabilizing selection via trade-offs with other life history traits. Because of the expectation of trade-offs among life history traits (and therefore stabilizing selection), it seems to me that the simple version of the inbreeding approach will be relatively inefficient for such traits. In their original version of the paper Ketola et al. elected not discuss traits subject to stabilizing selection in any detail, something which was remarked upon by several of the reviewers. As a result, they have now pointed out that the inbreeding method can be applied even to traits subject to stabilizing selection by using an interaction index. I think this is a valuable addition to the paper.

Another potential problem with this approach is epistatic variance. Inbreeding will convert epistatic variance to additive genetic variance, and this additive genetic variance will not have been subject to direct selection. Changes in trait values as a result of epistatic variance exposed via inbreeding might therefore not show any signature of directional dominance, even if the trait of interest actually has been subject to directional selection. When I originally wrote my review of Ketola et al., I didn’t have any examples of empirical data involving extensive inbreeding-mediated epistatic effects. However since then, a very interesting paper has been published demonstrating precisely this phenomenon in Drosophila melanogaster (Huang et al., 2012). Huang et al. showed that there was no overlap in significant SNPs (single-nucleotide polymorphisms) for a suite of quantitative traits between a set of 40 sequenced inbred lines (the Drosophila Genetic Reference Panel or DGRP; Mackay et al., 2012) and an outbred population (Flyland) derived from these inbred lines. However the majority of the SNPs identified in the Flyland population participated in at least one epistatic interaction in the DGRP dataset. They concluded that epistasis dominates the genetic architecture of quantitative traits in Drosophila. In their reply to my original review of their paper, Ketola et al. pointed out that although it is known that epistasis can create some non-linearity between inbreeding depression and the inbreeding coefficient, no strong deviation from linearity has previously been found (Lynch and Walsh, 1998). They therefore argued that epistatic interactions are unlikely to play a major
confounding role in deducing fitness effects via inbreeding depression. Although Huang et al.’s approach has its own limitations—for example that the outbred Flyland population was reconstituted from the set of inbred genotypes and therefore much deleterious recessive variation has presumably already been purged—these results suggest that epistatic effects may be more important and pervasive than previously thought. It is unknown whether epistatic variance will affect the change in the mean of a trait after inbreeding, whether it will only cause a change in variance of the trait, or whether epistatic effects will result in unpredictable changes in both the mean and the variance as a result of inbreeding. It is only in the first case that the results of the inbreeding method will no longer be reliable. However it seems clear that this is an issue worthy of further empirical study.

Despite these caveats the method proposed is interesting and potentially very useful, and I look forward to seeing it applied more frequently in future, as a result of the publication of Ketola et al.’s paper.

REFERENCES


