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NEWS AND COMMENTARY

Stronger selection on males

Are males the more 'sensitive' sex?

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Deleterious alleles constantly enter populations through mutation. The presence of these alleles in populations results in a 'mutational load' (Haldane, 1937; Mullller, 1950), such that individuals are, on average, less fit than they would be otherwise. We are particularly interested in the extent to which females suffer from mutation load, because females typically determine population productivity. Several authors have argued that females may experience a reduced load, because they benefit from being part of a gene pool that is purified at the expense of males (Manning, 1984; Kodric-Brown and Brown, 1987; Whitlock and Agrawal, 2009). This requires that selection against deleterious alleles be stronger on males than on females—a theoretically appealing idea with limited direct evidence. Mallet and Chippindale (2011) provide additional support to this idea by showing that inbreeding depression (ID) for fitness in *Drosophila melanogaster* is considerably stronger in males than in females.

Although much attention has been given to cases involving conflicting selection pressures between the sexes, this situation likely represents the exception rather than the rule. Most new mutations are probably deleterious in both sexes. In a female, a typical mutation will directly or indirectly reduce her health and thus her fecundity. In a male, the same mutation will reduce his health and thereby limit his ability to search for mates, compete with rivals and vigorously court females. The high variance in male mating success that results from competition for mates means that selection can potentially be much stronger in males than in females (Wade, 1979).

Ideally, one would measure the fitness effects of individual mutations in each sex to confirm that deleterious alleles typically experience stronger selection in males than in females. However, direct measures of selection on individual genes are extremely laborious, and have mostly been limited to studies involving a small number of phenotypically visible mutations (Whitlock and Bourguet, 2000; Pischedda and Chippindale, 2005; Sharp and Agrawal, 2008; see also Hollis *et al*., 2009). Such gene-level studies have typically supported the notion that male fitness is more sensitive to genetic perturbations than female fitness, but broader support is desperately needed.

An alternative approach is to study a more representative sample of naturally occurring variation by measuring selection against inbred genotypes. In this context, inbred genotypes can be thought of as genotypes of 'low genetic quality' relative to outbred genotypes. ID can be viewed as the strength of selection against inbred genotypes. Mallet and Chippindale, by using the cytogenetic tools of *Drosophila*, isolated haplotypes that they then expressed in outbred genotypes or in a state of near-complete homozygosity, thus maximizing their power to detect selection. Moreover, they were able to obtain excellent measures of fitness because their assay conditions closely resembled the conditions under which their lab population has evolved for many generations.

For juvenile fitness, measured as larval viability, ID was about 35% in both sexes. However, ID in adult fitness was much stronger and differed between the sexes. Adult male fitness was considerably more sensitive to inbreeding than adult female fitness, with ID estimates of 90% for males but only 64% for females. The observation that selection against inbred genotypes is similar between the sexes at the juvenile stage but different at the adult stage suggests that sexual selection, broadly defined, is responsible for the stronger selection that occurs on males.

These results are all the more remarkable given that approximately 20% of the genome is on the X chromosome. X-linked genes cannot contribute to ID in males, because both inbred and outbred males will be hemizygous for such genes. However, X-linked genes can contribute to ID in females. Thus, if selection were equivalent in the two sexes, we would expect more selection against inbreeding in females than in males simply because of the larger number of genes. For this reason, the difference in ID between the sexes may underestimate the difference in selection.

Attributing the difference in ID between the sexes to the difference in selection assumes that the dominance coefficient h is the same for both sexes. By relating the homozygous and heterozygous fitnesses, Mallet and Chippindale were able to infer that average dominance was very similar across the two sexes. Thus, it is unlikely that the difference in ID is because of a difference between the sexes in the degree to which deleterious effects are recessive. Furthermore, their results indicated that deleterious effects on adult fitness components in both sexes tended to be considerably more recessive than those on juvenile fitness. This curious result may warrant further study, given that the vast majority of estimates of dominance come from studies of *D. melanogaster* in which larval viability is the only measure of fitness. However, caution is needed in interpreting the estimates of dominance reported by Mallet and Chippindale, as the estimation procedure makes a number of assumptions about the nature of segregating variation.

Using inbreeding to create genotypes of low genetic quality exploits naturally occurring deleterious alleles. However, a limitation of this approach is that the actual genes contributing to ID are unknown. In principle, it is possible that a different set of genes contribute to ID for male fitness than for female fitness. If that is the case, then these results would be misleading with respect to the idea that female fitness can be improved by the elimination of alleles through selection on males. However, Mallet and Chippindale found a strong positive correlation between the sexes across inbred haplotypes, suggesting that the set of genes affecting the two sexes was highly overlapping.

These results provide an important new piece of evidence that is consistent with the idea that most mutations affect males and females in the same direction, but that selection tends to be stronger in males. Historically, much effort has been spent on understanding elaborate secondary sexual traits and female preferences. The work reported by Mallet and Chippindale is part of a growing interest in thinking more broadly about sexual selection and its consequences on the genome at large (Whitlock and Agrawal, 2009).

Conflict of interest

The author declares no conflict of interest.

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