Extra-Pair Copulations and Associated Genetic Benefits

Introduction

Extra-pair copulations (EPCs) occur when animals engage in sexual relationships outside of the social pair bond and produce broods of mixed paternity. This promiscuity is prevalent in many species that were previously viewed as monogamous, thus it has become evident that monogamous pairs of animals are not always sexually exclusive. As a result, social monogamy does not reflect sexual or genetic monogamy- actually, it has been shown that extra-pair offspring are found in approximately 90% of avian species **(Griffith et al.).**

In this review, I will present evidence that the genetic benefits to females of EPCs often are more complicated than what can be gained by mating with the highest-quality male. Instead of choosing the highest 'quality' male, females instead benefit by choosing mates that are genetically dissimilar in their Major Histocompatibility Complex (MHC) genes**,** as this choice can provide genetic benefits in terms of increased immuno-capacity to offspring **(Von Schantz et al.)**. This type of opposite-attraction mate-choice applies to taxonomically diverse lineages, including fish (**Lenz et al.)** birds (**Brouwer et al.)**, and humans **(Chaix et al.).**

EPCs with males offer adaptive functions through phenotypic and genotypic benefits to the female and her offspring. Phenotypic benefits may include parenting assistance by the extra male and possible courtship feedings, whereas genotypic benefits may include acquiring higher quality paternal genes for the offspring from the extra-pair male, increased genetic diversity of the brood and guaranteed fertilization. Extra-pair mating provides an excellent opportunity to investigate the indirect genetic benefits of female choice, because comparisons between within-pair offspring (WPO) and extra-pair offspring (EPO) can be made. By controlling the non-genetic effects of the rearing environment and maternal effects- the differences between the maternal half –siblings should be due to genetic differences between the sires.

MHC genes are found in all vertebrates and are the most polymorphic genes in vertebrate genomes. They play key roles in immune function by coding for cell-surface glycoproteins that control antigen presentation to T- lymphocytes **(Griggio et al.).** Therefore, measuring levels of polymorphism at these genes can provide indirect measures of the immunological fitness of populations. Increased MHC diversity increases the potential for an organism to have immunity to more infections, highlighting why the MHC locus is an important criterion in female mate choice.

Extensive research continues to investigate the genetic benefits of EPCs dependent on MHC allelic diversity. Most EPCs involve extra-pair males that have higher MHC diversity than cuckolded males from the mating pair. This offers genetic benefits to the offspring through increased MHC diversity; however, no overall consensus has been reached about the adaptive significance of EPCs in female birds. This review will delve into the controversial and inconsistent literature surrounding the adaptive significance of EPCs dependent on MHC variability. I will highlight findings that support the idea that there are genetic benefits of MHC-dependent EPCs, as well as the discrepancies regarding the proximate mechanisms for how females select extra-pair males. It is widely agreed that MHC genes are influential factors of female mate choice, yet the mechanisms through which females make their choices are elusive.

Mechanistic debate: How do females select males based on genetic quality? Competing theories:

1. **Good Genes Hypothesis:** Females gain advantageous alleles from males through choosing those with certain phenotypic traits.
    - **Von Schantz, Y et al**. Paper supports the 'good genes' hypothesis that females discriminate among MHC characteristics in males on the basis of secondary sexual characters (spur length in Pheasants) in order to pass on genes for disease resistance that improve fitness in their offspring.

2. **Complimentary Hypothesis:** Females select males with particular MHC qualities depending on their own genotype.
    - **Brouwer et al.** They may seek the best combination of maternal and paternal MHC genes to improve offspring MHC characteristics: females may prefer to mate with males with the most dissimilar set of MHC genes so as to maximize offspring MHC diversity or they may choose males with which they share an intermediate number of MHC alleles so as to optimize offspring MHC diversity at an intermediate level
    - **Freeman et al.** Although several studies support the idea that EPCs allow females to obtain 'good genes' for their offspring, many others have found no relationship between female mating fidelity and traits likely to reflect male quality. This study shows that females do use EPCs to increase the quality of young, but it is the interaction between maternal and paternal genomes that is the target of female choice. This is the 'genetic compatibility' hypothesis and was tested in a free-living population of Savannah sparrows. Females sought complementary genes for their offspring, which suggests that the benefits of heterozygosity at the MHC drive female mating patterns.
    - **Aeschilmann et al.** This hypothesis is also supported by the fact that Stickleback fish use self-reference in mate choice: they use information about their own and their potential mate's MHC polymorphism for optimal complementation of their own set of alleles.
3. **Both Good Genes and Complimentary Hypotheses play a role:** Female mate choice may be a complex of both of these mechanisms.
    - **Roberts and Gosling (2003).** Although MHC dissimilarity (complimentary hypothesis) and a 'good genes' indicator (investment in urine scent-marking) both have a role in determining female preference, their relative influence can vary depending on the degree of variability in each trait among available males.
    - **Lenz et al.** Overall, this study found mate choice for intermediate MHC diversity, *i.e.* compatible genes, and found only indirect evidence for the occurrence of good genes in MHC by comparing the data with an earlier study.

Evidence that MHC diversity increases immune functioning

- **Loiseau et al.** MHC diversity/ heterozygosity reduces infection rate by the Malaria parasite *plasmodium reticulum* in house sparrows: In three cases, the presence of an allele was associated with a decreased risk to harbor the infection.
- **Ujvari et al.** Genetic diversity at MHC genes may protect against the spread of contagious cancers in wild populations of animals.

The Benefits of MHC-dependent EPCs

Because EPCS are costly to the females, there must be benefits from this behavior that outweigh the costs **(Schmoll).**

1. **Increased MHC diversity in EPO**
   Brouwer et al. In the Seychelles Warbler, EPO are more MHC diverse than WPO because selected EP males have higher MHC diversity than cuckolded (original male partner) males. By gaining EPCs, females originally paired with low MHC-diversity males are ensuring that their offspring do not end up with below average levels of MHC diversity and therefore lower survival.

2. **Increased Immunity and Survival in EPO**
   Johnsen et al. Evidence that extra-pair mating in bluethroats (*Luscinia svecica)* can improve the individual immune response (immuno- competence) of EPO nestlings. This suggests not only a genetic benefit from an extra-pair mating preference, but also an interaction effect of maternal and paternal genotype on offspring immunocompetence (supports compatibility hypothesis).

3. **Prevents inbreeding**
   It is thought that EPCs that involve extra-pair males with different MHC diversity will decrease the extent of inbreeding and reduce detrimental effects associated with inbreeding depression in animals. Thus, this can be seen as another adaptive outcome of MHC-dependent EPCs.
   - **Freeman et al.** In Savannah Sparrows, avoidance of inbreeding by choosing males with more diverse MHC alleles may also be an ultimate cause of social and genetic mate choice for MHC- dependent EPCs.
   - **Aeschilmann et al.** The self-referential allele-counting hypothesis used by females predicts that MHC-based mate choice favors dissimilar MHC alleles in males in small populations facing the risk of inbreeding.

Recent Findings on Genetic Benefits: EPCs are Context-Dependent

1. **Environmental variation could obscure the genetic benefits of EPCs**
   - **Garvin et al.** It was found that EPCs provide females with offspring with superior immune responses as the T-cell-mediated immune response of EPO was stronger than that of WPO in common yellowthroats (*Geothlypis trichas*). However these results were only significant in the colder of the two years; immune response was related positively to air temperature and nestlings had a stronger immune response in the warmer year.

2. **The effects of differential maternal investment in relation to paternity and environmental conditions:**
    - **Schmoll.** These factors are largely not accounted for in the majority of EPC studies and relevant environmental variation may include the time of breeding in temperate regions, hatching order and offspring sex. Maternal effects could arise as selection may favor females with the ability to bias resource allocation in favor of offspring descending from preferred, higher quality genetic EP males.

Difficulties with the study of MHC-dependent EPCs

1. **In many cases, there are no phenotypic traits that portray genotypic qualities such as MHC diversity.**
    - **Promerova et al.** No correlation between the diversity of MHC alleles and condition-dependent traits such as body mass and tarsus length or expression of a secondary sexual ornamentation in males. This is despite the fact that the carotenoid-based feather ornament has already been proved to govern reproductive success in this species.

    How do females discriminate between males with varying MHC alleles?

    - Olfaction
        i. Urine scents in mice: cues regarding MHC similarity are mediated by urinary odor. Androgen-dependent urinary odor cues advertise male status or are seen as "good genes" indicators of quality **(Roberts et al. 2003).**
        ii. Body odor in humans: Cycling women tested during the follicular phase of their menstrual cycles rated odors of MHC-dissimilar men as more pleasant than odors of MHC-similar men. Additionally, odors of MHC-dissimilar men more often reminded women of current or previous partners, indicating that odor plays a role in partner choice. **(Roberts et al. 2008)**
    - Visual and auditory cues in birds: Anatomical, electrophysiological and behavioral data are shown, demonstrating that birds in general possess a functional olfactory system and are able to use olfactory information in a variety of ethological contexts, including reproduction. **(Balthazart and Taziaux 2009).**
    - Post-copulatory immunological mechanism: There is a possibility that females use select sperm after copulation, which eliminates the need for any phenotypic cues to male genotype. **(Johnsen et al.)**

Conclusion

There have been a plethora of studies done regarding EPCs and genetic benefits in terms of MHC diversity; however, the specific adaptive benefits, the mechanisms of female mate choice and environmental effects on both of these are still inconclusive. Interestingly, the lack of consideration of environmental factors on genetic benefits of

EPCs in many studies harkens to the infamous nature-nurture issue, and the fact that the effects of genes and the environment are not mutually exclusive. It has been shown that there are genetic benefits of EPCs that involve MHC diverse genes. However, there are a multitude of other studies with strong data sets supporting that EPC females target EP males with higher quality genes, but have inconclusive results regarding the direct genetic differences in the EPO compared to WPO. Additionally, some studies do not offer support that females even choose EP males of higher genetic quality. The results from both of these inconclusive cases may be more supportive if they are re-analyzed in context with the environment.

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