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Commentary: Paternal and maternal influences on offspring phenotype: the same, only different

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In mammals, the female provides substantially more reproductive investment than the male. Biologists have long wondered why exactly this should be so. According to Dawkins and Carlyle, the answer is simply that, with internal fertilization, males get the first opportunity to default on parental care, and females are left, quite literally, holding the baby.[1] Whether or not males actually provide parental care can then be negotiated: marmoset males provide a lot, even undergoing pregnancy weight gain to fund their postnatal care,[2] whereas hedgehogs offer nothing. In teleost fish, for whom fertilization is external, it is the females who vanish after laying the eggs and the males who provide doting parental care.[1] In energetic terms, female mammals have a much greater 'reproductive energy burden' than males, but it has also been proposed that this gives them, as the 'physiological niche' of pregnancy and lactation, much greater influence over early offspring development.[3] Female mammals also tend to invest greater effort in decisions regarding mate selection and mating schedule.[3]

Biologists are therefore encouraged to think of the two parents as contributing equally genetically to mammalian offspring, but differentially in terms of physiological nurturing during the periods of gestation and lactation, with mothers occupying a privileged role. This perspective prompts an immediate question: how much extra influence on the offspring's phenotype is gained by the mother through pregnancy and lactation? In this issue, Vik and colleagues address this question in the context of parent-offspring associations in cardiovascular risk factors, and come to the conclusion that maternal physiology counts for almost nothing.[4] The magnitudes of the two parental influences on offspring phenotype are almost identical, and the authors conclude that the influence of intrauterine physiology is 'minor compared with the influences of conventional genetics and/or the shared environment'.[4]

This is not the first time that the effect of maternal physiology has been proposed to be minimal, e.g.[5] but if we dig beneath the surface it rapidly becomes clear that there is almost no way in which the two parents exert equal phenotypic effects on their offspring; rather, there is an accumulation of unequal effects from each parent. If the accumulations of inequality sum to relatively equal parent-offspring correlations in phenotype for mothers and fathers, then it may not necessarily be because intrauterine influences are unimportant; they may simply be offset by other pathways and mechanisms.

Conventional wisdom is that both parents contribute genetically to each trait in the offspring on an equal basis. But this picture is simplistic: studies of chimeric embryos, in which the genetic contribution of one parent has been artificially doubled, show that the paternal genome contributes disproportionately to muscle tissue and less to the brain, whereas the maternal genome shows the opposite pattern.[6] Contrasts are also apparent within the brain: the paternal genome makes a dominant contribution to hypothalamic structures, whereas maternal genes contribute disproportionately to the cortex, striatum and hippocampus.[7] Keverne and colleagues proposed that such contrasting parental effects may be associated with complex patterns of primate brain evolution, with a trend characterized by expansion of the female-dominated part at the expense of the male-dominated part.[7]

At the level of specific loci, a proportion of genes are imprinted and only expressed according to whether they are of paternal or maternal origin. A paternally-imprinted gene inherited by a woman from her father would be

silenced, but would still be expressed on transmission to the next generation since it would now be of maternal origin. The evolution of genomic imprinting has been attributed to a tug-of-war between the two parents over the level of maternal investment during pregnancy and lactation, on the assumption that paternal genes, uncertain of being in future offspring of the same mother, favour a greater transfer of resources than maternal genes.[8] Other explanations for imprinting have also been offered, such as improving coordination between placental physiology and brain development, again important in primate encephalization trends.[9] Each of these explanations acknowledges first the challenge of allocating resources to the offspring during development, and second that the two parents have different optimal strategies in this context.

At the time of conception, the ovum is substantially greater in size than the sperm and contributes more cytoplasmic material to the offspring, both genetic and non-genetic.[10] From this point onwards, the mother's physiological influence has traditionally been assumed to dominate. Maternal diet around the time of conception, and pregnancy physiology and pathogen load, have all been shown to influence offspring phenotype. A particularly elegant approach has been to contrast the metabolic phenotype of successive offspring before and after their mothers develop diabetes or undergo obesity surgery.[11,12]

Yet the notion that pregnancy gives maternal phenotype primary influence on the offspring can be contested both theoretically and empirically. From a theoretical perspective, it has been noted that maternal phenotype acts to buffer the offspring from ecological stresses.[13] For example, pregnant mothers substantially dampen the effects on their offspring of both famine and spikes in nutritional supply.[13] By smoothing short-term and unreliable signals of ecological conditions, the mother provides a more coherent niche during the most sensitive period of development.[13] In turn, this means that the offspring is exposed to 'maternal capital',[14] and to a significant extent this refers to maternal genotype or traits shaped by developmental experience. From an empirical perspective, studies of both animals and humans suggest that paternal phenotype can influence that of the offspring through epigenetic imprinting of the sperm.[15–17] Similar to the tug-of-war enacted through genomic imprinting, therefore, fathers may promote ecological imprints on the offspring whereas maternal pregnancy physiology seems to act to constrain them.[18]

But we haven't dug deep enough yet. The ovum contributed by a mother to her offspring develops decades earlier and is present during the mother's own fetal life.[19] In this way, each ovum is exposed to grand-maternal phenotype (which may, according to the logic expressed above, bear a strong imprint of grand-maternal genotype and developmental phenotype). As yet, less is known about the developmental profile of imprinting of sperm, but prospermatogonia do undergo methylation in fetal life.[20] What happens during subsequent cell divisions merits further research, and it is not yet clear whether non-genetic information transmitted by the father primarily reflects ecological conditions at the time of the offspring's conception, or paternal fetal exposure to grand-maternal phenotype. Paternal age at offspring birth is associated with offspring telomere length, but the evidence is inconsistent across studies as to whether this paternal effect is stronger than any such maternal effect, or vice versa.[21]

Finally, these contrasting parental influences on the offspring are prone to vary according to the quality of the environment. When environmental quality is high, the effect becomes homogeneous. Given a 'level playing field', therefore, genes paradoxically exert greater influence on phenotype, and traits become more heritable. It remains to be seen if the results of Vik and colleagues would be reproduced in a population subject to substantial between-individual variability in living conditions.

Our understanding of how each parent impacts on offspring phenotype remains incomplete, and apparent equality of co-variance between offspring and their mothers vs fathers may not tell us everything about the relative influence of any specific biological process, such as pregnancy or lactation.

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