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Genetic Basis of Intrapsychic Conflict

Robert L. Trivers

The connection between Bob Trivers and Dan Freedman dates back to the mid-1970s, coincident with the publication of Edward O. Wilson's book, Sociobiology: The New Synthesis *(1975).*[1] *This new discipline, which examines the biological bases of social behavior with reference to evolutionary concepts and principles, sparked considerable controversy. Its challenges to traditional beliefs about the origins of human social behavior excited those who believed that psychological analyses needed a bioevolutionary component. In response to the promptings of colleagues, Freedman arranged to meet Trivers during a visit to Harvard University. He "learned much about sociobiology from Trivers" during their first short session together. The two currently share an interest in the nature and origins of internal conflict.*

This chapter examines the novel concept that internal psychological conflict may have a genetic basis. This idea is explored with reference to the

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[1] The introduction to this chapter was written by the editors of this volume.

recently discovered phenomenon of genomic imprinting—in other words, the differential expression of certain genes in offspring dependent on whether inheritance of these genes is maternal or paternal. Genomic imprinting is viewed as the *major advance in understanding kinship since Hamilton's (1964a, 1964b) theory of kin selection, and it leads to a series of predictions regarding internal psychological conflict that may affect interactions with relatives.*

GENETIC SOURCES OF CONFLICT

There are probably many sources for internal conflict in humans, including some that are classically mapped on to parent–offspring interactions in which at least one parent is represented by a strong internal "voice." Recently, there has been compelling evidence of a novel source of inner conflict that is genetic. This is initially very surprising because humans consist of genetically identical somatic cells working for the gonads, and there is no conflict expected between them. The liver and the kidney, for example, are not in conflict over how many resources to remove from the bloodstream, because they are all genetically identical, nonreproductive, and working for the gonads. As evolutionary researchers have understood from Hamilton's (1964a, 1964b) kinship theory, however, they are also working with reference to other individuals, such as close relatives, attempting to confer benefits and avoid conferring costs.

The nutshell of the present argument is that within an individual *genetic elements do not all enjoy the same degree of relatedness to a close relative.* In the case of two full brothers, the Y chromosome "sees" the pair as being identically related. The autosomes only "see" them as half related, so there is a possibility for conflict, over evolutionary time and within a single individual, between these genetic elements. Over evolutionary time it is possible to imagine a mutant on the Y chromosome that says, in effect, "Treat brothers as if they are identical twins, but neglect sisters." (Sisters and brothers have no overlap of self-interest because sisters lack the Y chromosome.) Mitochondrial DNA says, "Value only sisters because

only sisters pass on mitochondrial DNA." Two full brothers share identical mitochondrial DNA, but neither reproduces it, because mitochondrial DNA is only transmitted from mother to progeny.

A Y mutant such as described above could appear and should start to spread if located on the appropriate genetic element. However, if it did, it would immediately set up a selection pressure on the much larger array of autosomal genes to counteract this spread—in other words, to "turn off" the Y chromosome mutant. This process is conflict over evolutionary time, but could be resolved in an individual's psyche or physiology, as well. This is because there are competing elements generated by these different genes that may compete for control of the individual.

Until recently, the outline of the preceding argument was understood, but imagined to be unimportant because the genetic elements referred to are minority elements in the extreme. The Y chromosome is approximately 1% of the genome by amount of DNA, but it is mostly inert. It has very few functioning genes per unit length compared to the autosomes or to the X chromosome. Thus, individuals have considerably less than 1% of the genes available on "that side of the fight" versus all of the autosomes "united against it." Mitochondrial DNA is one tenth of 1% of total DNA, so it is also a minority element.

In the past 5 years, it has been exciting to understand that autosomes do not act in unison. Instead, paternal genes (genes inherited from the father) are in some circumstances in conflict with maternal genes (genes inherited from the mother). There is the same kind of evolutionary conflict based on differing self-interest and the same possibility for internal conflict, and that is the focus of the following discussion.

GENOMIC IMPRINTING

The phenomenon that has been discovered is called *genomic imprinting* (see Barlow, 1995). Genomic imprinting leads to exact degrees of relatedness through each parent instead of probabilistic degrees of relatedness. (This concept is addressed again later.) These exact degrees of relatedness

mean that genes can act according to parent of origin, "on behalf of father" or "on behalf of mother." This leads to quite disparate degrees of relatedness—in other words, the difference between 1/2 and 0, as will be demonstrated. Furthermore, there is now abundant evidence that there are forms of internal physiological conflict within single individuals, which map on to these two opposing genetic elements. Remember that these are not minority elements, but rather half of the autosomes versus the other half of the autosomes. In a female, this process also includes her X chromosomes, so that the paternal X and maternal X chromosomes are in some expected disagreement. In principle, all of a female's genome, leaving aside the mitochondrial DNA, are involved in an antagonistic interaction by parent of origin.

What is the phenomenon? Genomic imprinting refers to what is also sometimes called *parent-specific gene expression.* A classic assumption of Mendelian genetics, which is true for the vast majority of genes, is that a gene in an individual is active in the same way regardless of which parent contributed it. In other words, the gene is the same stretch of DNA with no information "left over" from the transmission. Thus, if one is a heterozygote for eye color (brown being dominant and blue being recessive), the individual will have a brown phenotype regardless of which parent contributed the genes. Genomic imprinting refers to a small minority of known genes that have the property of being expressed in an individual only if inherited from a particular parent. Thus, there are paternally active genes, genes that are active in a person only if donated by the father. A mother could donate the identical set of DNA at that locus; however, it is inactivated, or *imprinted.* (Imprinting refers to the negative state, but because the present intent is to model the active state it is easier to use the language of paternally active and maternally active genes.)

There are, in turn, genes active in an individual only if donated by the mother. Think back to the eye color locus to see how it works. If the gene is paternally active and one received the brown allele from the father, the phenotype would be brown (blue is the recessive trait). However, if an individual received the blue allele from the father, the brown eye allele from the mother is inactivated and the blue phenotype is expressed. In

other words, the phenotype is different even though the genotype is identical.

IMPLICATIONS OF GENOMIC IMPRINTING FOR KINSHIP THEORY

It was the brilliance and beauty of David Haig, an Australian evolutionary biologist who received his PhD in the 1980s, to recognize that *genomic imprinting has very striking implications for measuring degrees of relatedness* (Haig, 1992, 1993; Haig & Trivers, 1995). This observation escaped the notice of geneticists who resisted learning about kinship theory. It is instructive to review this process with reference to interactions between hypothetical half-brothers.

If individuals have a common mother, then the old-fashioned way of measuring degrees of relatedness (e.g., as taught in *Social Evolution,* Trivers, 1985) comes from the work of Hamilton (1964a, 1964b). Specifically, a nonimprinted gene in one son (half-sibling 1) has a 50 : 50 chance that it came from the mother and a 50 : 50 chance that it came from the father. This is what is meant by a probabilistic degree of relatedness—in other words, no additional information is available. If the gene is in the mother, she passed it to her other son (half-sibling 2) 50% of the time ($1/2 \times 1/2 = 1/4$). Imagine, instead, that this is a paternally active gene; the active state of an allele is now being modeled so the effects of the gene when inactive can be disregarded for the moment. The following argument can be made: The gene is active in half-sibling 1 and it is a paternally active gene. Therefore, it is known that it came from the father *and,* therefore, is not present in half-sibling 2. The two half-siblings have different fathers so the degree of relatedness for the paternally active genes is 0. In contrast, if the gene were maternally active it would be active in half-sibling 1 and so would have come from the mother. There is a 1/2 chance the mother passed the gene to half-sibling 2; hence, $r = 1/2$, so the old-fashioned degree of relatedness of 1/4 for a half-sibling can be seen as an average of the degree of relatedness of 1/2 through the mother and 0 through the father.

The difference between 1/2 and 0 is considerable. Cancer researchers or molecular biologists attempt to explain imprinting in terms of cancer, as a device to prevent asexual reproduction, and various other inappropriate events (Haig & Trivers, 1995). They think that cancer is a big selection pressure. However, it is known that cancer is a relatively weak selection pressure, but the difference between 1/2 and 0 starting at the beginning of life is considerable. An example, using mice, illustrates how this process works. It is known that mouse siblings in utero are a mixture of half- and full siblings; typically, a mother mates with at least two different males per litter. (In the interest of simplicity, every offspring and every future offspring are designated as half-siblings.) In the case of half-siblings 1 and 2, in utero, if the gene is not imprinted, it says they are related by 1/4, on average, so the relationship is valued by 1/4. However, if it is paternally active it says, "We are not related, nor am I [half-sibling 1] related to any of my mother's future progeny, they mean nothing to me, genetically speaking." Therefore, paternally active genes are expected to be associated with greater parental investment from mother, faster growth in utero, larger size at birth, increased aggressivity in interactions with siblings, and other similar characteristics. Maternal genes are expected to be exactly the opposite.

There are three organisms in which genomic imprinting has been studied in some depth: mice, humans, and corn. Mice and humans map almost exactly on to each other. The rule for mice (which is statistically significant in different cases) is this: Paternally active genes or paternally active gene regions (areas in which the gene has not yet been located but in which a paternally active gene is known to be present) are associated with more rapid fetal growth rates, larger size at birth, greater suckling motion, and other comparable features. Maternally active genes tend to have the opposite effect.

Moreover, a parallel fact comes from flowering plants such as corn, and the structure of interest here is the endosperm, which is a triploid structure. The point is slightly more complicated to argue, but the logic is essentially the same. There are little ovules that are pollinated by pollen that are coming partly from at least two other plants. Therefore, there is

a mixture of half- and full siblings on each cob that is especially important for paternally active genes. Paternally active genes, or gene regions, are associated with large, fat kernels of corn stuffed with resources. In contrast, maternally active genes are associated with kernels that tend to be shriveled and small, or devoid of certain nutrients.

The foregoing provides the basic theory and it extends to all kinship interactions, not just the early mother–offspring interactions on which Haig concentrated (Haig & Trivers, 1995). Most of the genes described are early acting genes, but the selection process applies to any kin interaction. For example, it is a fact that in ground squirrels, females often give warning calls. Females also tend to be half-sisters much of the time, and female kinship is important in nature. This means that the maternal genes of a female are going to make for closer relations to these other females, while the paternal genes are going to make for more distant relations. Maternal genes might be expected to lead to cries of, "Squawk! Squawk!" when a predator approaches, whereas paternal genes might be expected to lead to a little burst of internal fright. "Keep quiet!" They might say, "Remember yourself and get to your burrows!"—which is what a paternal gene is closer to representing under these circumstances.

PHYSIOLOGICAL AND PSYCHOLOGICAL CONFLICTS

There are exact examples of internal physiological conflicts. The following is a model for what psychological conflicts might look like.

Igf2 and *Igf2r* are the most amazing pair of genes in terms of this story (Haig & Graham, 1991). They are found in both humans and mice. In mice, *Igf2* (insulin-like growth factor-2) increases rates of mitosis, increases rates of cell division, increases growth rates, and increases body size at birth by 40%. It is paternally active. To put it differently, if a disrupted form of the paternal allele is inherited so that neither is operating in the offspring, the maternal one having been silenced by imprinting, the result is a dwarf that is 40% smaller but is otherwise perfectly proportioned (see Haig & Trivers, 1995).

Igf2r is insulin-like growth factor 2 receptor. However, it is not a receptor in the conventional biochemical sense of being the receptor through which *Igf2's effects* are activated. Its function is to take certain chemicals into the lysosome and degrade them. It evolved in mammals, after the evolutionary divergence from the lineage leading to chickens, a secondary binding site for *Igf2*. Its effect is to remove *Igf2* from the bloodstream and to degrade it. It reduces body size by 25% to 30%, and it reduces circulating levels of *Igf2* by a factor of 2.7 (Lan et al., 1994). In other words, the result is exactly what would be expected if internal conflict is a reality—a kind of inefficient system that nearly ends up back at the center point. (It actually has a slight upward bias, itself an interesting fact.) However, it is almost a wash, and these are strong counter-posing selection pressures.

Examples of possible psychological conflicts are important to explore. I will begin with a theoretical possibility of internal conflict concerning inbreeding. I will then review interesting evidence suggesting that the body is relatively *more maternal* in some sections and relatively *more paternal* in other sections—in other words, that it has relatively more paternally (or maternally) active genes expressing themselves in different tissues, hence the tissues themselves may be in conflict, including physiological conflict (especially in the brain).

Imagine you are contemplating a sexual encounter with your first cousin and guiding your thoughts with reference to evolutionary logic. The inbreeding increases the degree of relatedness to any resulting child, which gives a genetic benefit, but it also increases the homozygosity of the child, which imposes a cost (inbreeding depression). But you are inevitably related to your cousin on one side of your genome and not the other (absent parental inbreeding). If your cousin is your mother's brother's child, then your *maternal* genes are closely related (usually $r = 1/4$), whereas your paternal genes are unrelated ($r = 0$). Hence, both sets of genes suffer the cost of inbreeding depression, but only the maternal genes enjoy an increase in relatedness.

Given the foregoing, the maternal side of the self may be saying, "You know kissing cousins are cute, especially when there is a resemblance on the mother's side," whereas a moralistic tone might be generated by the

paternal genes: "But what about the defects generated?!" It is in this manner that internal psychological conflict associated with these degrees of relatedness can be envisioned.

Another informative example involves chimeric mice. Chimeric mice are a mixture of normal mice cells, fertilized in the normal way, with cells introduced very early in development such that they form a coherent developing fetus for almost a full term. The relative propagation rates of the different cell types can be studied. There is an introduction of gynogenetic cells—in other words, asexually reproduced via mitosis from a female. Such cells only have a double set of maternally active genes and no paternally active genes. Alternatively, something called androgenetic cells are introduced. These have a double dosage of genes inherited from the male, but none from the female, so they have two sets of paternally active genes and no maternally active genes. A set of these very recent experiments show that different parts of the body end up with relatively paternally active cells or maternally active cells that can be intuitively linked to the underlying logic of imprinting (Fundele & Surani, 1994).

A skeleton tends to have more paternally active cells and genes. It is the skeleton that has to first enlarge and elongate if the body is to increase in size. This is one function paternally active genes tend to "want" to perform, at least early in development. The neocortex and most of the brain are maternally active; only the hypothalamus is paternally active. There are just evolutionary guesses as to what is taking place, but one possibility is that those same kinship decisions discussed earlier (e.g., "Do I give a warning call, whom do I nurse, how much do I let her into my territory, is that my aunt or my half-aunt, or my first cousin or my second cousin?") are mostly maternal decisions, so the cognitive processes undergirding them in the neocortex might be expected to be maternal. The hypothalamus regulates growth, but it also regulates appetite; thus, the more egocentric, "numero uno" factor may operate here. In an internal argument, the neocortex might be saying metaphorically, "Family is nice, family is important, I like family," whereas the hypothalamus might answer, "Me first!" or "I'm hungry!"

THE X CHROMOSOME

Paternally active and maternally active X chromosomes in women are especially interesting. In a woman's body, as in a female mouse body, a given X chromosome is turned off in any given cell. Tissues tend to have both kinds of cells so that women have both X chromosomes active in the tissue. However, there are whole stretches of cells (as is known with respect to coat color in calico cats) that have only one or the other X chromosome expressing itself. It has now been shown in mice that there are bands of brain cells that are relatively maternally active, then paternally active, then maternally active, not unlike streaks or bands going across the cortex (Tan et al., 1995). Are they sometimes in conflict, as expected, over appropriate behavior?

SUMMARY AND SOME FURTHER THOUGHTS

The foregoing certainly suggests the possibility of internal conflicts directed by different sets of cells—for example, alternating bands of brain cells. The X chromosomes have especially interesting properties in regard to genomic imprinting, but further discussion of this particular phenomenon is beyond the scope of the present chapter. In summary, a critical point is that the most important advance in understanding kinship since Hamilton's work is genomic imprinting. This is because genomic imprinting changes how all the fundamental degrees of relatedness are assessed. It changes how one measures the degree of relatedness to the parent. It is an inevitable consequence of this twist on kinship theory that there should be, and almost certainly is, internal conflict run by the gene expressing itself physiologically. It seems certain that this process will eventually be demonstrated psychologically as well.

The mechanism of genomic imprinting is still poorly understood. Methylation of DNA is involved in some way, but cause and effect are uncertain. There are, presumably, genes involved in imprinting other loci; some tentative evidence has been put forward regarding mice.

A final point is that, in this work, two people who have the same genome are *not* compared. The same genes can be inherited from each

parent, but apparently something epigenetic, either a protein bound to DNA or a difference in methylation status (hypermethylated or hypomethylated) is involved. Some factor has to be passed down, and it is not the DNA genetic structure itself. It will be important to watch for new developments over the next several years that will enhance understanding of this intriguing process.

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