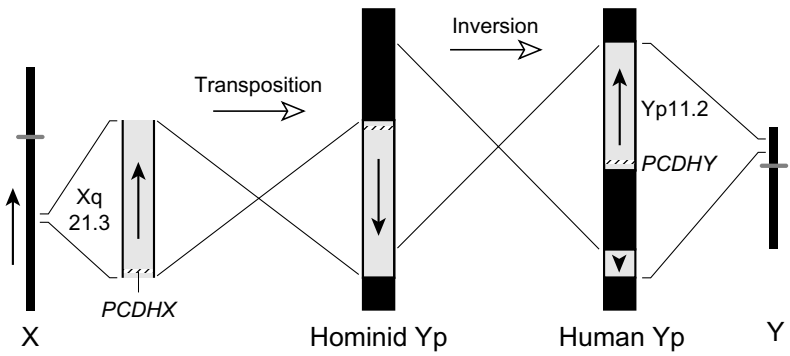
# III

# THE SEARCH FOR A CRITICAL EVENT

Sex chromosomal rearrangements as putative speciation events in hominid evolution




The origin of the Xq21.3/Yp regions of homology in *Homo sapiens* by a reduplicative translocation dated at between 3 and 2 million years BP and a subsequent (and presently undated) paracentric inversion that split the translocated block on a hominid Y short arm. Adapted from Schwartz A. et al (Reconstructing hominid Y evolution: X-homologous block, created by X-Y transposition, was disrupted by Yp inversion through LINE-LINE recombination. Human Molecular Genetics 1998; 7: 1-11) to show the location of the protocadherin XY gene (PCDHX and PCDHY - see chapter by Sargent et al).

# Sexual Selection, Timing and an X–Y Homologous Gene: Did *Homo sapiens* Speciate on the Y Chromosome?

TIM J. CROW

**Summary.** A theory of the speciation of modern *Homo sapiens*, that a single gene played a critical role in the transition from a precursor species, is founded upon the following. (1) The premise that hemispheric asymmetry is the defining feature of the human brain and the only plausible correlate of language. (2) An argument for a specific candidate region (the Xq21.3/Yp11.2 region of homology) based upon the reciprocal deficits associated with the sex chromosome aneuploidies, and the course of chromosomal change in hominid evolution (supported by a weak linkage to handedness). A gene (protocadherinXY) identified within this region is expressed in the brain with the potential to account for a sex difference. (3) A particular evolutionary mechanism (sexual selection acting on an X–Y-linked gene) to account for species-specific modification of what initially was a saltational change (in this case a chromosomal rearrangement). These postulates relate to the case of modern *H. sapiens*; on the basis of the recent literature it is argued that (3) has general significance as a mechanism of speciation.

## THE ORIGINS OF THE CONCEPT

THE CONCEPT (Crow, 1998a, b, 2000a) developed from two origins.

1. The theory of M. Annett, who has argued for a number of years (Annett, 1978, 1985, 1995) that her single gene theory of the genetics of cerebral asymmetry (the right-shift theory) is the key to the evolution of the human characteristic of language.
2. Arguments concerning the aetiology of psychosis, specifically that the most puzzling feature of schizophrenic psychoses (the central paradox; Crow, 2000b) is that these illnesses occur with approximately the same

*Proceedings of the British Academy*, **106**, 197–216, © The British Academy 2002.

> incidence in all populations in spite of being associated with a substantial biological (fecundity) disadvantage. It seems that the condition is intrinsic (and therefore in some sense 'genetic') in origin. Why are the relevant genes not selected out of the population?

In 1984 I concluded that a previous environmental theory (contagion; Crow, 1983) of the aetiology of schizophrenic psychosis was untenable. What was required to explain the universal incidence and the brain changes associated with the disease was genetic diversity related to the trajectory of human brain development (Crow, 1984). On the basis that we had found that a component of the brain change was asymmetrically distributed to the hemispheres (Brown *et al.*, 1986), I formulated the hypothesis that the relevant genetic variation was that associated with the asymmetry gene that Annett had argued was responsible for the specifically human developments of the anatomy of the brain. Further evidence (Crow, 1986, 1990) for deviations in asymmetry of the structural changes accumulated, but I was puzzled by a number of sex differences [for example in age of onset, and the tendency towards same-sex concordance, i.e. affected relatives are more frequently of the same sex than would be expected, as had been noted earlier by Penrose (1942) and Rosenthal (1970)]. These influences of sex appeared to require a genetic explanation, but given the observation that illness may be transmitted from an affected father to a child of either sex, a conventional sex-linked pattern of inheritance of predisposition was excluded. To overcome this problem I proposed (Crow, 1988; see also Crow, 1987) a locus within the pseudoautosomal region. Within this region there is recombination between X and Y chromosomes in male meiosis, with the consequence that there is strict homology of genes on the X and Y. This provided an explanation of same-sex concordance (Crow *et al.*, 1989) but, as I now appreciate, on account of the strict X–Y sequence homology, it provided no explanation of a sex difference.

A more radical hypothesis was required. This came from consideration of the psychological impairments associated with the sex chromosome aneuploidies; these deficits are consistent with the location of a gene for cerebral asymmetry within a region of X–Y homology. While I had first proposed (Crow, 1989) a pseudoautosomal locus (i.e. for cerebral dominance as well as psychosis), a more satisfactory theory (Crow, 1993), because it could account for the sex differences associated with psychosis and cerebral asymmetry, was that the gene was located within one of several sex-specific (i.e. non-pseudoautosomal) regions of X–Y homology that had by that time been well described (Page *et al.*, 1984) and located with respect to primate phylogeny (Lambson *et al.*, 1992).

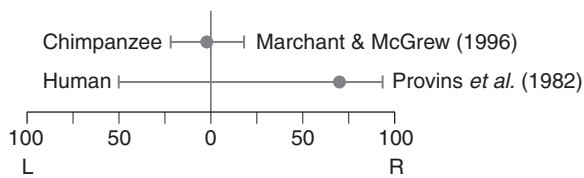
## CEREBRAL ASYMMETRY AS THE SPECIES-DEFINING FEATURE

In writing a commentary on Annett's right-shift theory (Crow, 1995), it occurred to me that the theory could be more forcefully stated. If her claim, that the right shift was the defining characteristic of the human brain, was sustained, the conclusion had implications for speciation theory: the genetic change that generated the right shift should be considered as a speciation event. Annett (1995) had argued that population-based directional asymmetry of handedness was specific to *H. sapiens*, and had presented evidence that it was absent in the gorilla (Annett & Annett, 1991). The conclusion was substantially reinforced by the studies of Marchant & McGrew (1996) of chimpanzees in the Gombe National Park (and by the cross-species studies of Holder, 1999). In reviewing the primate literature, McGrew & Marchant (1997) concluded that:

> nonhuman primate hand function has not been shown to be lateralised at the species level—it is not the norm for any species, task or setting, and so offers no easy model for the evolution of human handedness.

The contrast is illustrated by the comparison of hand usage for the everyday range of activities in the chimpanzee and human (Figure 1).

There is a discontinuity. Directional asymmetry is present in the human but absent in the great ape population. When can this discontinuity have arisen? Clearly sometime between the separation of the hominid and chimpanzee lineages, i.e. between approximately 5 million and 100,000 years ago (the minimal estimate for the origin of modern *H. sapiens*; Stringer & McKie, 1996). The change must have had a genetic basis. The juxtaposition places Annett's theory




| | Number of Individuals | Activities |
|---|---|---|
| Chimpanzee | 38 | 46 |
| Human | 1960 | 75 |

**Figure 1.** Hand preference in chimpanzees and humans compared. Data for chimpanzees refer to a community of wild chimpanzees (*Pan troglodytes schweinfurthii*) observed in the Gombe National Park by Marchant & McGrew (1996). Data for *Homo sapiens* were collected by questionnaire from populations of undergraduate psychology students in Scotland and Australia by Provins *et al.* (1982). Medians and boundary values (95%) have been extracted from the graphs of the original publications.

within an evolutionary context, albeit one, the nature of speciation, associated with controversy.

Thus formulated, the case of *H. sapiens* raises questions for speciation theory (see also the introduction to these *Proceedings*). Both the concept that the gene is associated with persisting and in part disadvantageous variation (that I was trying to account for in the case of psychosis, and Annett argued for in her heterozygote advantage hypothesis), and a location for the gene on the sex chromosomes, such as I was arguing for, have implications for the mechanism of transition from a precursor species. What was the origin of variation maintained at an apparently constant rate against a selective disadvantage? What were the implications of a sex difference in a novel species characteristic? Did the sex chromosomes have a special status with respect to the genetics of speciation?

## WHAT DOES HAND SKILL PREDICT?

In her heterozygote advantage hypothesis, Annett argued that if the right-shift factor was the key change in *H. sapiens*, a relationship with cognitive ability would be expected. This has been a controversial prediction (Table 1).

By the balance of papers the consensus is negative, cognitive ability is unrelated to hand skill. But this consensus hides a multitude of methodological differences between studies. Some that reached positive conclusions (for example

**Table 1.** Does hand skill predict cognitive ability?

| Positive | Equivocal | Negative |
|---|---|---|
| Levy (1969) | | |
| Miller (1971) | | |
| | | Calnan & Richardson (1976) |
| | | Hardyck *et al.* (1976) |
| | Harshman *et al.* (1983) | McManus & Mascie-Taylor (1983) |
| Annett & Kilshaw (1984) | | |
| Annett & Manning (1990) | | Bishop (1990) |
| | Whittington & Richards (1991) | |
| | | McManus *et al.* (1993) |
| | | Palmer & Corballis (1996) |
| | | Resch *et al.* (1997) |
| Crow *et al.* (1998) | | |
| | | Cerone & McKeever (1999) |

Levy, 1969; Miller, 1971) used samples of modest size. A number of studies that reached negative conclusions (Calnan & Richardson, 1976; McManus & Mascie-Taylor, 1983; Bishop, 1990; Whittington & Richards, 1991) did so on the basis of the large sample (more than 12,000 individuals tested at the age of 11 years) included in the UK National Child Development study. But these studies made use of the records on the 'hand that the child writes with' rather than a quantitative index.

We (Crow *et al.*, 1998) re-examined the issue in the same data set but constructed a quantitative index of 'relative hand skill' based upon the numbers of squares the child ticked with each hand in 1 minute. This analysis revealed deficits not so much at the extremities of hand skill, as Annett had suggested, but close to the point of equal hand skill (ambidexterity), as Orton (1937) and Zangwill (1960) predicted. Those around the point of 'hemispheric indecision' were impaired on verbal (Figure 2) and other abilities relative to those who were more strongly lateralised either to the right or to the left.

Thus lateralisation determines a component of ability close to the core of language. A dimension of variation persists in the population that is related to the characteristic that defines the species. Moreover, the dimension can be accounted for by a relatively simple genetic influence.

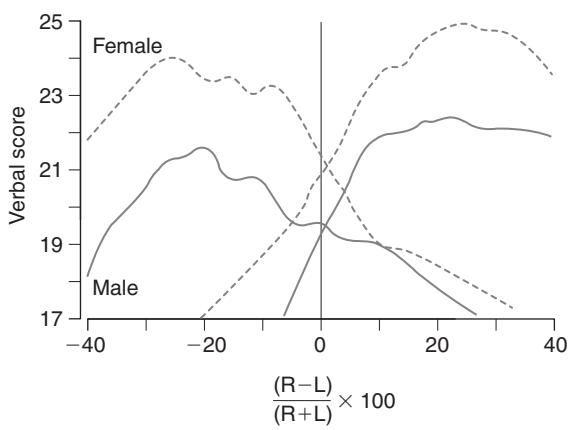



**Figure 2.** Relationship between verbal ability and relative hand skill (Relhand) in left- and right-hand writers (plotted separately) in 11,700 individuals in the National Child Development cohort for whom data at age 11 years were available. The curves have been smoothed with a Lowess function and truncated at Relhand values of −40 and +40, or where the numbers of individuals at a particular Relhand value discrepant with writing hand became too small to sustain the function (reproduced from Crow *et al.*, 1998).

## THE CASE FOR AN X–Y HOMOLOGOUS GENE

Where is the gene? Sex differences for verbal ability are documented (Maccoby & Jacklin, 1975; Halpern, 1992) and illustrated in Figure 2: females have an advantage over males. There is also a sex difference for degrees of handedness: females are more strongly right-handed than males and are less likely to be left-handed (Annett, 1985; McManus, 1991; Crow *et al*., 1998). It is plausible that these sex differences are related and that both in turn are related to the sex difference in brain growth: brain development is faster in females than in males (Figure 3).

The key to the genetics of asymmetry lies in the neuropsychological deficits associated with the sex chromosome aneuploidies (Crow, 1993). Individuals who lack an X chromosome (XO or Turner's syndrome) have relative deficits of non-dominant hemisphere capacity (performance IQ), while individuals with an extra X chromosome (XXY or Klinefelter's syndrome and XXX syndrome) have relative deficits of dominant hemisphere capacity (verbal IQ) (Netley & Rovet, 1982; Netley, 1986). As XXY individuals are male and XXX individuals are female, these effects cannot be attributed to gonadal hormones.

These findings indicate that a gene on the X chromosome influences the relative development of the hemispheres. The fact that deficits comparable to those in Turner's syndrome are not present in normal males, who, like Turner's syndrome individuals, have only one X chromosome, indicates that the gene must also be present on the Y chromosome. This argument generates the hypothesis that the asymmetry factor belongs to the class of X–Y homologous genes. Consistent with the theory, a tendency for handedness to be associated

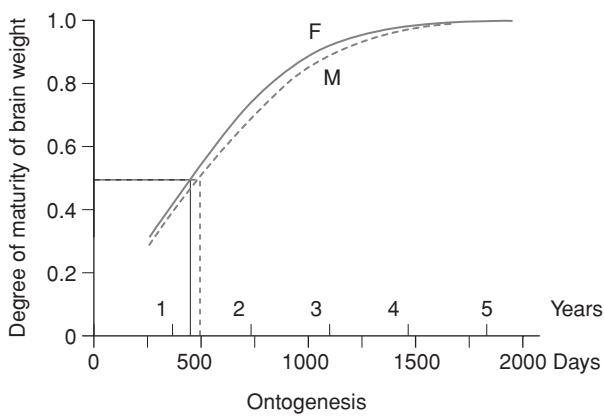



**Figure 3.** The sex difference in brain growth. From Kretschmann *et al.* (1979).

within sibships with sex (same-sex concordance) was observed in a collection of 15,000 families (Corballis *et al*., 1996). Whereas the earlier version of the hypothesis (Crow, 1989), that the gene was within the pseudoautosomal region, did not explain a sex difference (such as those noted above), the later hypothesis (Crow, 1993), that it is located in a sex-specific region of homology, does so because the lack of recombination within such a region allows sequence variation on the Y to occur independently of that on the X chromosome.

McKeever (2000) has presented an analysis of the literature and a new family sample in support of a gene on the X chromosome, but discounts a locus on the Y chromosome on the grounds of Corballis' (1997) argument that a stable polymorphism on the Y would not be maintained within the population. However, the evidence summarised above from sex chromosome aneuploidies, the presence of a same-sex concordance effect and, given an X chromosomal locus, the fact of father to son transmission, all support such a locus. An alternative to Corballis' assumption that the variation on the Y chromosome is related to the DNA sequence (the basis of his rejection of the X–Y theory) is presented below.

## THE SIGNIFICANCE OF THE Xq21.3 TRANSLOCATION AND THE Yp PARACENTRIC INVERSION

Genes that are present in homologous form on the X and the Y chromosomes were predicted to account for the phenomena of Turner's syndrome by Ferguson-Smith (1965). Their presence has been formally demonstrated within the pseudoautosomal region (Rouyer *et al*., 1986; Rappold, 1993) and within the sex-specific region of the Y (Page *et al*., 1984). In general, these regions have arisen as a result of translocations to the Y chromosome from the X. The evolutionary time–course of these chromosomal rearrangements has been charted by Lambson *et al.* (1992) (see the later chapter in these *Proceedings* by Carole Sargent *et al.*).

The regions of greatest interest with respect to evolutionary developments in humans are those that have been subject to change between the chimpanzee and *H. sapiens*. Two regions, the Xq21.3/Yp region of homology (Sargent *et al*., 1996; Mumm *et al*., 1997) and the 0.4 Mb pseudoautosomal region (PAR 2) at the telomeres of the long arms of the X and Y, stand out. Both representations on the Y chromosome were established after the separation of the hominid and chimpanzee lineages. Of these two, a gene within the Xq21.3/Yp region more readily explains a sex difference on the basis that sequence divergence can take place within the sex-specific regions of the X and Y but not within PAR 2.

The time–course of these changes is of great interest. The translocation from Xq21.3 to Yp has been estimated, on the basis of X–Y sequence divergence, at

approximately 3 million years (Sargent *et al*., 1996; Schwartz *et al*., 1998). This was followed by a paracentric inversion, which has not been dated, that split and reversed the block in Yp, and by a series of changes within the homologous region around DXS214 (for details see the chapter by Carole Sargent *et al*.; Sargent *et al.*, 2001). It will be important to determine the temporal sequence of these changes in so far as this can be reconstructed. One question that can be asked about each variation is whether the change is universal in extant human populations. Where this is the case, as for the original translocation, the paracentric inversion and the changes at DXS214, the change has potential relevance to species-defining characteristics. One must assume that in each case the change has been selected. Beyond that it occurred after the separation of the chimpanzee and hominid lineages, no information has so far been obtained for the origin of pseudoautosomal region 2.

## NEOTENY AND THE PLATEAU OF BRAIN GROWTH

How could these changes have influenced the evolution of language and *H. sapiens*? As Chaline *et al*. (1998) have pointed out, the morphological differences between the skulls of the great apes and those of the hominid series can be accounted for by a series of changes: (1) retreat and verticalisation of the face; (2) an increase in cranial capacity; and (3) tilting of the foramen magnum. These changes are apparent in landmark comparisons of skull outlines for the great ape and *Australopithecus* with *Homo erectus* and *H. sapiens* (Figure 4).

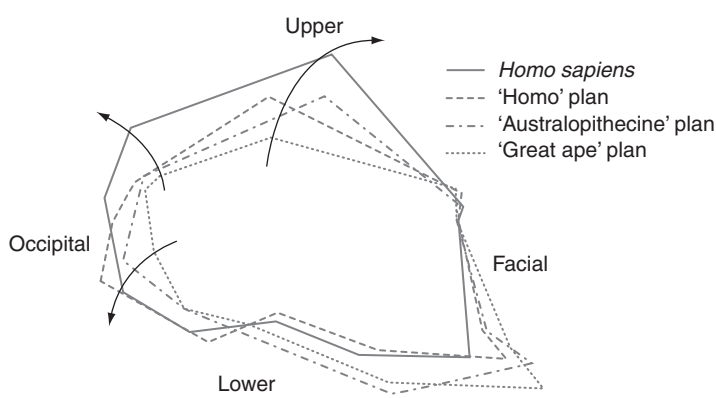



**Figure 4.** Comparisons of landmark-based skull outlines in *Homo sapiens*, hominids, Australopithecines and great apes. From Chaline *et al.* (1998).

The relative complexity of the differences between the adult skull outlines is much reduced in a comparison of the juvenile morphology of the great ape with *H. sapiens* (Figure 5).

The contrast is consistent with Bolk's (1926) concept that *H. sapiens* evolved by a process of neoteny, the prolongation into adult life of some features that are characteristic of infancy in a precursor species. In *H. sapiens* the topology of the skull, including the recessed conformation of the face (relative to that of the adult ape), is retained into the adult form. As Bolk suggested, it seems likely that this occurred by a process of 'heterochrony', a change in the relative timing of the components of development. In *H. sapiens* the development of the skull relative to the soma (into the topology of the adult chimpanzee) does not take place.

What selective factor could account for such a delay? It is implausible (and it does not seem to have been seriously argued) that there is selection for the facial features of infancy. What is surely more likely is that the facial features of the infant ape are retained in humans as a consequence of selection for some other characteristic, and that this characteristic relates to the brain itself rather than to its casing.

Holt *et al*. (1975) drew attention to the fact that in different primate species brain weight increases *pari passu* with body weight and then reaches a plateau. Across species the trajectory of brain growth is similar but the point of plateau differs, it is delayed in the chimpanzee relative to the macaque and in humans relative to the chimpanzee. A genetic change that accounted for the transition from one plateau to another could be at the core of the difference between two species (Figure 6).

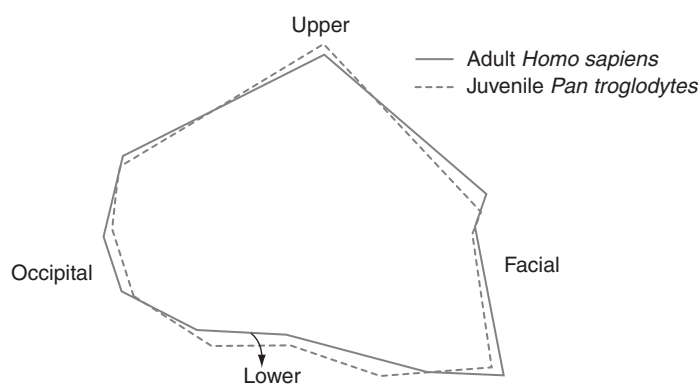



**Figure 5.** From Chaline *et al.* (1998).

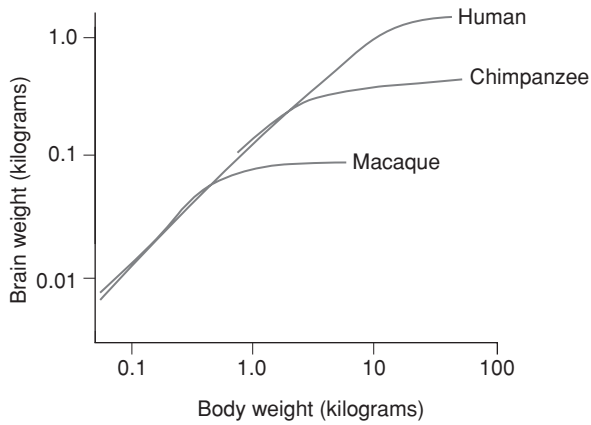



**Figure 6.** Brain weight in relation to body weight. From Holt *et al*. (1975).

## SEXUAL SELECTION AS A MODIFIER

A critical change on the sex chromosomes, specifically one that it is located within a sex-specific region of homology between the X and the Y, introduces a new consideration, that the change will be differentially represented in the two sexes. There are two reasons why this is the case. First, in the case of a translocation from the X to the Y, such as has occurred with the Xq21.3/Yp block, the dosage in males will be double that in females (and also that in males who lack the translocation) because genes on one X chromosome are normally inactivated (see below). Secondly, lack of recombination between the X and the Y opens up the potential for sequence divergence. Either mechanism could lead to a sex difference in gene expression. Whatever its origin (gene dosage or sequence difference), such a sexual dimorphism is open to differential modification by mate choice.

Sexual selection can modify the primary change, first in males and then in females, and this modification proceeds along the dimension of variation that has been introduced by the initial change. Thus a novel sexual dimorphism becomes the focus of differential selection in the two sexes. The potential for quantitative change, constrained by the nature of the genetic innovation, enables a search for a new equilibrium. In the case of a rate-regulating process, for example the point of plateau in brain development, the attainment of the new equilibrium may be associated with a series of secondary adjustments, for example to facial morphology, as exemplified by neoteny in humans.

The hypothesis that speciation takes place as a consequence of sex chromosomal change followed by sexual selection overcomes two of the problems that saltational theories encounter. The first difficulty is explaining how an organ-

ism that has been subject to a discontinuous change can acquire a mate. According to the present theory the change occurs first in one individual in one sex, a male, and the innovation is then propagated to the progeny of that individual by a process of selection by females. Later there is a process of modification of the critical sequence or its expression in females as the males carrying the new sequence on their Y chromosomes increase in the population. Successive modification of the gene or its expression first in males and then in females appears to conform to the process of runaway sexual selection envisaged by Fisher (1930) and Lande (1981).

The second difficulty for saltational theories is to explain how a single discontinuous change can become integrated into a coherent and viable new form (the 'hopeful monster' problem; Goldschmidt, 1940). The present theory accounts for such integration on the basis that the single change (chromosomal or genetic) within a region of homology on the Y chromosome initiates a phase of sexual selection and heterochronic adjustment that equilibrates in a new plateau of maturation. This plateau will be associated with a changed suite of developmental trajectories (orientated around the core process) and its own sexual dimorphism. Thus a saltational change in a single male is selected by females and the effects (expressed through both X and Y copies of the gene) are modified by mate choice in both sexes. In this way a primary change in a rate-determining gene on the Y chromosome allows mate selection to determine a new playing field of sexual encounter.

A key question is the genetic consequence of the change on the Y chromosome for the original gene on the X chromosome. Genes on one X chromosome in females are subject to X inactivation, the process (dosage compensation) whereby the quantitative expression of genes on the X is equalised in males and females. A gene in a block on the Y that has transposed from the X is in an unusual situation, it escapes from X inactivation and is expressed in double dosage in the male. In general, one must suppose that an abrupt change in gene dose will be disadvantageous and that the great majority of such chromosomal rearrangements are rapidly selected out of the population. But in the case we are considering the relevant characteristic is positively selected and the gene on the Y is retained. In general it is observed that genes that are also present on the Y are protected from inactivation on the X (Davies, 1991), but the mechanism by which such protection is achieved is obscure. One possibility, that pairing of X and Y sequences in male meiosis plays a role (Crow, 1991; but see Burgoyne & McLaren, 1985), implies that the direction of the sequence on the Y relative to that on the X is significant, and therefore that in this case the paracentric inversion, which resulted in the realignment of X and Y sequences, is relevant. In discussing the differences between mammalian orders in the pattern of inactivation on the X of genes common to X and Y chromosomes, Jegalian & Page (1998) propose a mechanism that depends on successive changes (their figure 4)

in response to selective pressures (unspecified) on first male and then female fitness. This sequence could reflect the role of sexual selection in the course of mammalian speciation. Therefore it is possible that epigenetic modification of critical sequences on the X chromosome is a necessary component of the process of sexual selection that follows the rearrangements of the X and the Y chromosome that distinguish related species.

## SEXUAL SELECTION, SPECIATION AND SEX LINKAGE

The general concept that speciation and sexual selection are related has some support in the speciation literature. In attempting to explain the diversity of species of *Drosophila* on the Hawaiian archipelago, Kaneshiro & Boake (1987) concluded that the characteristics that differentiate species are those in which a change in a sexually dimorphic feature has become subject to mate choice. Similar arguments have been developed to account for the rapid speciation and diverse coloration of cichlid fish in the lakes of East Africa by Dominey (1984) and McKaye (1991), and in relation to song, morphology and plumage in birds by Price (1998). In each case it is argued that sexual selection has a role in generating pre-mating isolation of a new species from its precursor. Language in *H. sapiens* can be considered as an examplar of this sequence (Crow, 1996).

Other authors (Ringo, 1977; West-Eberhard, 1983; Turner & Burrows, 1995; Zink, 1996; Kaneshiro, 1997; Carson, 1997) have discussed aspects of the relationship between sexual selection and speciation. The thread of continuity in these discussions is that change in some identifiable characteristic associated with one sex initiates a process of sexual selection that separates the species. Here it is proposed that the genetic foundation of this sequence (as applied to mammals) is that a primary change in the Y copy of an X–Y homologous gene (1) generates a novel sexual dimorphism and (2) is subject to female choice, and that the X–Y difference becomes the target of a process of sexual selection with the runaway characteristics described by Fisher (1930).

## PATERSON'S SPECIFIC MATE RECOGNITION CONCEPT

These conclusions are relevant to a definition of a species that casts new light on both the isolation or 'biological' species concept and the saltational theory: Paterson's (1985) specific mate recognition concept, the notion that what defines a sexually reproducing species, and differentiates one species from another, is the mechanism for recognising a mate (Lambert & Spencer, 1994). Paterson (1985) defined a species as 'that most inclusive population of individual, bi-parental organisms which share a common fertilisation system'. The

specific mate recognition concept has been described as a 'fundamental property of a species, established at the time of speciation, and essentially unaltered thereafter' (Turner, 1994).

Sex chromosomal change has relevance to the concept. A change on the sex chromosomes can introduce novelty into the mate recognition system that is open to rapid and differential modification in the two sexes. In discussing the role of chromosome change in speciation in Hawaiian drosophilids, Carson (1970) considered the possibility that 'the founder event may be accomplished by a single propagule, probably a single fertilized female', although he later (Carson, 1997) modified this view in judging that 'genetic effects might produce a species by one or a few catastrophic steps … to be an unrealistic expectation'. According to the concept outlined here, the primary change is on the Y chromosome, and the founder event occurs in a male.

Paterson (according to Carson, 1995) argued that reproductive success within each species is well served by a:

> specific mate recognition system comprising a number of co-adapted stages. The co-adaptation referred to is intersexual: a signal from one potential sex partner evokes a particular response from the other; these events may then culminate in a chain of alternating signals between the individuals resulting in the success or failure of copulation.

Such a description may be applied, in the case of *H. sapiens*, to language.

## CONCLUSIONS

The asymmetry of the human brain is a feature that is not shared by other primates. It is variable between individuals, and this variation influences the acquisition of words, arguably the core feature of the species-defining characteristic of language.

On the basis of the neuropsychological deficits associated with the sex chromosome aneuploidies, an X–Y homologous gene for asymmetry was proposed, and is supported by the transmission of handedness within families. Such a gene can explain the sex difference in verbal and other aspects of cognitive ability and the faster development of the female brain; it will be subject to sexual selection. According to this concept the human brain evolved by a process of neoteny (delayed maturation) under the influence of mate choice for ability to communicate.

The speciation of modern *H. sapiens* is proposed as an instance of sexual selection acting on recent sex chromosomal change to establish a new 'specific mate recognition system': language. A change in a region of X–Y homology introduces novelty into the mate recognition system that is open to rapid and

differential modification in the two sexes. A candidate region in *H. sapiens* is that block of sequences within Xq21.3 that transposed to the Y chromosome short arm after the separation of the chimpanzee and hominid lineages and was subject to a subsequent paracentric inversion in Yp; a candidate gene is protocadherinXY, expressed in different forms on the X and the Y chromosomes. The role for X–Y homology postulated in sexual selection and speciation draws attention to epigenetic regulation of such genes as relevant to the understanding of speciation-related variation and pathologies.

## DISCUSSION

**Questioner:** There seems to be a selective advantage to the choice of right-hand lateralisation: one hand for eating and one for cleaning the body. Are there any cross-cultural studies of handedness?

**Crow:** The best cross-cultural studies are by Perelle & Ehrman (1994). There are some problems with these data, but they conclude that the population-based direction of the right-handedness is consistent across cultures.

**Skuse:** As you know, we've been interested in sex chromosome aneuploidies and we've studied 100 females with Turner's syndrome. According to Marian Annett's theory, the proportion of left-handers should be somewhat greater than 10% in the general population. The proportion of left-handers in the Turner's girls is exactly the same as that with females with normal X chromosomes.

**Crow:** I'm not supporting all aspects of Marian Annett's theory, but what you also show is the same finding that has been in the literature from the work of Money (1964, 1993), that is deficits of spatial ability in Turner's individuals. You find that irrespective of whether the X chromosome comes from the mother or the father.

**Skuse:** No, that's not exactly right.

**Crow:** That's strong evidence that there is an asymmetry factor there.

**Skuse:** I wouldn't interpret it that way. You are absolutely right, there are verbal advantages relative to performance deficits, it's about 80%, not 100%. In Klinefelter's syndrome most people would say there is an overall disadvantage, but the level of IQ is somewhat lower than what you've shown there.

**Crow:** But it's the relative IQ (see also Netley, 1998).

**Skuse:** Yes, you're absolutely right. There's something to be explained there. But the way you have explained it is that there's a speciation event which

involved a block of X-linked genes transferred to the Y and then an inversion occurring a half million years ago. But how can something happening on the recombining part of Y chromosome explain what is happening on the X chromosome? How does what has led to asymmetry in the male lead to the equivalent change in women?

**Crow:** That's where, if it works at all, sexual selection has to come in. So you've got a new situation where there is a desirable characteristic selected for first by females and then by males.

**Questioner:** Are you saying there are two separate events: one on the Y and one also occurring on the X?

**Crow:** Yes. I accept that because I think the prediction is that not only should there be divergence on the Y but the gene on the X should now diverge from the gene on the primate X with which we can compare it. The divergence may be in the sequence or it may be in the epigenetic modification of its expression.

**Wolpert:** Within the terminology of Bickerton, there is protolanguage and language. Would you say that within these specific mate recognition systems it is necessary to have a language system rather than a protolanguage? We are talking here about the emergence of linguistic abilities and it seems unclear why a language rather than a protolanguage would be a preferential mate recognition system.

**Crow:** I don't see that this is a problem; both of them could be selected for.

**Questioner:** Are you saying that one pre-mutation in a stone age man gave us language? No evolutionary biologist would explain why echolocation is present in bats on the basis of one pre-mutation. No evolutionary biologist would explain sonar contact in whales in the same manner. There have to be selection pressures.

**Crow:** Let me explain the implications of a chromosomal event such as this. Clearly it has been selected. This is not on the Y in a chimpanzee. It is on the Y in every human male. It is possible that there are no genes in this region, in which case it will be completely neutral. Then it would be like heterochromatin on the Y and of no consequence at all. But if there are genes in this region then the translocation and paracentric inversion must have affected their control and expression first in males then in females as I have described. At some stage there was positive selection. It is extremely interesting that this translocation is what got selected. What we imagine is that many such changes on the sex chromosomes may occur and then get lost because they are not advantageous and are selected out. But this is exceptional; somewhere within this block the sequence is noteworthy because that is what has survived.

**Wolpert:** So are you saying that the first person to speak was a male and that this person was a famous person in that way?

**Crow:** Yes.

## References


Annett, M. (1978) *A Single Gene Explanation of Right and Left Handedness and Brainedness*. Coventry: Lanchester Polytechnic.

Annett, M. (1985) *Left, Right. Hand and Brain: The Right-shift Theory*. London: Lawrence Erlbaum.

Annett, M. (1995) The right-shift theory of a genetic balanced polymorphism for cerebral dominance and cognitive processing. *Current Psychology of Cognition*, **14**, 427–80.

Annett, M. & Annett, J. (1991) Handedness for eating in gorillas. *Cortex*, **27**, 269–75

Annett, M. & Kilshaw, D. (1984) Lateral preference and skill in dyslexics: implications of the right-shift theory. *Journal of Child Psychology and Psychiatry*, **25**, 357–77.

Annett, M. & Manning, M. (1990) Reading and a balanced polymorphism for laterality and ability. *Journal of Child Psychology and Psychiatry*, **31**, 511–29.

Bishop, D.V. (1990) *Handedness and Developmental Disorder*. London: MacKeith.

Bolk, L. (1926) *Das Problem der Menschwerdung*. Jena: Gustav Fischer.

Brown, R., Colter, N., Corsellis, J.A.N. *et al*. (1986) Postmortem evidence of structural brain changes in schizophrenia. Differences in brain weight, temporal horn area, and parahippocampal gyrus compared with affective disorder. *Archives of General Psychiatry*, **43**, 36–42.

Burgoyne, P.S. & McLaren, A. (1985) Does X–Y pairing in male meiosis protect the paired region of the X chromosome from subsequent X-inactivation? *Human Genetics*, **70**, 82–3.

Calnan, M. & Richardson, K. (1976) Developmental correlates of handedness in a national sample of 11-year-olds. *Annals of Human Biology*, **3**, 329–42.

Carson, H.L. (1970) Chromosome tracers of the origin of species. *Science*, **168**, 1414–28.

Carson, H.L. (1995) Fitness and the sexual environment. In: *Speciation and the Recognition Concept* (eds D. M. Lambert & H. G. Spencer), pp. 123–37. Baltimore: John Hopkins University Press.

Carson, H.L. (1997) Sexual selection: a driver of genetic change in Hawaiian *Drosophila*. *Journal of Heredity*, **88**, 343–52.

Cerone, L.J. & McKeever, W.F. (1999) Failure to support the right-shift theory's hypothesis of a 'heterozygote advantage' for cognitive abilities. *British Journal of Psychology*, **90**, 109–23.

Chaline, J., David, B., Magniez-Jannin, F. *et al*. (1998) Quantification of the morphologic evolution of the Hominid skull and heterochronies. *CR Academy of Sciences Paris*, **326**, 291–8.

Corballis, M.C. (1997) The genetics and evolution of handedness. *Psychological Review*, **104**, 714–27.

Corballis, M.C., Lee, K., McManus, I.C. & Crow, T.J. (1996) Location of the handedness gene on the X and Y chromosomes. *American Journal of Medical Genetics (Neuropsychiatric Genetics)*, **67**, 50–2.

Crow, T.J. (1983) Is schizophrenia an infectious disease? *Lancet*, **342**, 173–5.
Crow, T.J. (1984) A re-evaluation of the viral hypothesis: is psychosis the result of retroviral integration at a site close to the cerebral dominance gene? *British Journal of Psychiatry*, **145**, 243–53.
Crow, T.J. (1986) Left brain, retrotransposons, and schizophrenia. *British Medical Journal*, **293**, 3–4.
Crow, T.J. (1987) Pseudautosomal locus for psychosis? *Lancet*, **2**, 1532.
Crow, T.J. (1988) Sex chromosomes and psychosis. The case for a pseudoautosomal locus. *British Journal of Psychiatry*, **153**, 675–83.
Crow, T.J. (1989) Pseudoautosomal locus for the cerebral dominance gene. *Lancet*, **2**, 339–40.
Crow, T.J. (1990) Temporal lobe asymmetries as the key to the etiology of schizophrenia. *Schizophrenia Bulletin*, **16**, 433–43.
Crow, T.J. (1991) Protection from X inactivation. *Nature*, **353**, 710.
Crow, T.J. (1993) Sexual selection, Machiavellian intelligence and the origins of psychosis. *Lancet*, **342**, 594–8.
Crow, T.J. (1995) The case for an X–Y homologous gene, and the possible role of sexual selection in the evolution of language. *Current Psychology of Cognition*, **14** , 775–81.
Crow, T.J. (1996) Language and psychosis: common evolutionary origins. *Endeavour*, **20**, 105–9.
Crow, T.J. (1998a) Sexual selection, timing and the descent of man: a genetic theory of the evolution of language. *Current Psychology of Cognition*, **17**, 1079–114.
Crow, T.J. (1998b) Why cerebral asymmetry is the key to the origin of *Homo sapiens*: how to find the gene or eliminate the theory. *Current Psychology of Cognition*, **17**, 1237–77.
Crow, T.J. (2000a) Did *Homo sapiens* speciate on the Y chromosome? *Psycoloquy*, **11**, 1.
Crow, T.J. (2000b) Schizophrenia as the price that *Homo sapiens* pays for language: a resolution of the central paradox in the origin of the species. *Brain Research Reviews*, **31**, 118–29.
Crow, T.J., Crow, L.R., Done, D.J. & Leask, S.J. (1998) Relative hand skill predicts academic ability: global deficits at the point of hemispheric indecision. *Neuropsychologia*, **36**, 1275–82.
Crow, T.J., DeLisi, L.E. & Johnstone, E.C. (1989) Concordance by sex in sibling pairs with schizophrenia is paternally inherited. Evidence for a pseudoautosomal locus. *British Journal of Psychiatry*, **155**, 92–7.
Davies, K. (1991) The essence of inactivity. *Nature*, **349**, 15–6.
Dominey, W.J. (1984) Effects of sexual selection and life histories on speciation: species flocks in African cichlids and Hawaiian *Drosophila*. In: *Evolution of Fish Species Flocks* (eds A. A. Echelle & I. Kornfield), pp. 231–49. Maine: Orino Press.
Ferguson-Smith, M.A. (1965) Karyotype–phenotype correlations in gonadal dysgenesis and their bearing on the pathogenesis of malformations. *Journal of Medical Genetics*, **2**, 142–55.
Fisher, R.A. (1930) *The Genetical Theory of Natural Selection*. Oxford: Oxford University Press.
Goldschmidt, R. (1940) *The Material Basis of Evolution*, reprinted 1982. New Haven: Yale University Press.

Halpern, D.F. (1992) *Sex Differences in Cognitive Abilities*. New Jersey: Lawrence Erlbaum.

Hardyck, C., Petrinovich, L.F. & Goldman, R.D. (1976) Left handedness and cognitive deficit. *Cortex*, **12**, 266–79.

Harshman, R.A., Hampson, E. & Berenbaum, S.A. (1983) Individual differences in cognitive abilities and brain organization. I. Sex and handedness differences in ability. *Canadian Journal of Psychology*, **37**, 144–92.

Holder, M.K. (1999) Influences and constraints on manual asymmetry in wild African primates: reassessing implications for the evolution of human handedness and brain lateralization (Dissertation Abstracts International Section A). *Humanities and Social Sciences*, **60**, 0470.

Holt, A.B., Cheek, D.B., Mellits, E.D. & Hill, D.E. (1975) Brain size and the relation of the primate to the non-primate. In: *Fetal and Post-Natal Cellular Growth: Hormones and Nutrition* (ed. D B. Cheek), pp. 23–44. New York: J. Wiley.

Jegalian, K. & Page, D.C. (1998) A proposed mechanism by which genes common to mammalian X and Y chromosomes evolve to become X inactivated. *Nature*, **394**, 776–80.

Kaneshiro, K.Y. (1997) RCL Perkins' legacy to evolutionary research on Hawaiian Drosophilidae (Diptera). *Pacific Sciences*, **51**, 450–61.

Kaneshiro, K.Y. & Boake, C.R.B. (1987) Sexual selection: issues raised by Hawaiian *Drosophila*. *Trends in Ecology and Evolution*, **2**, 207–11.

Kretschmann, H.F., Schleicher, A., Wingert, F., Zilles, K. & Loeblich, H.-J. (1979) Human brain growth in the 19th and 20th century. *Journal of the Neurological Sciences*, **40**, 169–88.

Lambert, D.M. & Spencer, H.G. (1994) *Speciation and the Recognition Concept: Theory and Application*. Baltimore: Johns Hopkins University.

Lambson, B., Affara, N.A., Mitchell, M. & Ferguson-Smith, M.A. (1992) Evolution of DNA sequence homologies between the sex chromosomes in primate species. *Genomics*, **14**, 1032–40.

Lande, R. (1981) Models of speciation by sexual selection on polygenic traits. *Proceedings of the National Academy of Sciences of the USA*, **78**, 3721–62.

Levy, J. (1969) Possible basis for the evolution of lateral specialisation of the human brain. *Nature*, **224**, 614–5.

Maccoby, E.E. & Jacklin, C.N. (1975) *The Psychology of Sex Differences*. Oxford: Oxford University Press.

McGrew, W.C. & Marchant, L.F. (1997) On the other hand: current issues in and meta-analysis of the behavioral laterality of hand function in nonhuman primates. *Yearbook of Physical Anthropology*, **40**, 201–32.

McKaye, K.R. (1991) Sexual selection and the evolution of the cichlid fishes of Lake Malawi, Africa. In: *Behaviour, Ecology and Evolution* (ed. M. H. A. Keenleyside), pp. 241–57. London: Chapman & Hall.

McKeever, W.F. (2000) A new family handedness sample with findings consistent with X-linked transmission. *British Journal of Psychology*, **91**, 21–39.

McManus, I.C. (1991) The inheritance of left-handedness. In: *Biological Asymmetry and Handedness (CIBA Foundation Symposium 162)* (eds Q. R. Bock & J. Marsh), pp. 251–81. Chichester: Wiley.

McManus, I.C. & Mascie-Taylor, C.G.N. (1983) Biosocial correlates of cognitive abilities. *Journal of Biosocial Science*, **15**, 289–306.

McManus, I.C., Shergill, S. & Bryden, M.P. (1993) Annett's theory that individuals heterozygous for the right-shift gene are intellectually advantaged: theoretical and empirical findings. *British Journal of Psychology*, **84**, 517–37.

Marchant, L.F. & McGrew, W.C. (1996) Laterality of limb function in wild chimpanzees of Gombe National Park: comprehensive study of spontaneous activities. *Journal of Human Ecology*, **30**, 427–43.

Miller, E. (1971) Handedness and the pattern of human ability. *British Journal of Psychology*, **62**, 111–12.

Money, J. (1964) Two cytogenetic syndromes. I. Intelligence and specific factor quotients. *Journal of Psychiatric Research*, **2**, 223–31.

Money, J. (1993) Specific neurocognitional impairments associated with Turner (45, X) and Klinefelter (47, XXY) syndromes: a review. *Social Biology*, **40**, 147–51.

Mumm, S., Molini, B., Terrell, J., Srivastava, A. & Schlessinger, D. (1997) Evolutionary features of the 4Mb Xq21.3 X–Y homology region revealed by a map at 60-kb resolution. *Genome Research*, **7**, 307–14.

Netley, C.T. (1986) Summary overview of behavioural development in individuals with neonatally identified X and Y aneuploidy. *Birth Defects Original Article Series*, **22**, 293–306.

Netley, C.T. (1998) Sex chromosome aneuploidy and cognitive developments. *Current Psychology of Cognition*, **17**, 1190–7.

Netley, C.T. & Rovet, J. (1982) Atypical hemispheric lateralization in Turner syndrome subjects. *Cortex*, **18**, 377–84.

Orton, S.T. (1937) *Reading, Writing and Speech Problems in Children*. New York: Norton.

Page, D.C., Harper, M.E., Love, J. & Botstein, D. (1984) Occurrence of a transposition from the X-chromosome long arm to the Y-chromosome short arm during human evolution. *Nature*, **331**, 119–23.

Palmer, R.E. & Corballis, M.C. (1996) Predicting reading ability from handedness measures. *British Journal of Psychology*, **87**, 609–20.

Paterson, H.E.H. (1985) The recognition concept of species. In: *Species and Speciation* (ed. E. S. Vrba), pp. 21–9. Pretoria: Transvaal Museum Monograph.

Penrose, L.S. (1942) Auxiliary genes for determining sex as contributory causes of mental illness. *Journal of Mental Science*, **88**, 308–16.

Perelle, I.B. & Ehrman, L. (1994) An international study of human handedness: the data. *Behaviour Genetics*, **24**, 217–27.

Price, T. (1998) Sexual selection and natural selection in bird speciation. *Philosophical Transactions of the Royal Society of London (Biological)*, **353**, 251–60.

Provins, K.A., Milner, A.D. & Kerr, P. (1982) Asymmetry of manual preference and performance. *Perceptual and Motor Skills*, **54**, 179–94.

Rappold, G.A. (1993) The pseudoautosomal regions of the human sex chromosomes. *Human Genetics*, **92**, 315–24.

Resch, F., Haffner, J., Parzer, P., Pfueller, U., Strehlow, U. & Zerahn-Hartung, C. (1997) Testing the hypothesis of relationships between laterality and ability according to Annett's right-left theory: findings in an epidemiological sample of young adults. *British Journal of Psychology*, **88**, 621–35.

Ringo, J.M. (1977) Why 300 species of Hawaiian *Drosophila*? The sexual selection hypothesis. *Evolution*, **31**, 694–6.

Rosenthal, D. (1970) *Genetic Theory and Abnormal Behaviour*. New York: McGraw-Hill.

Rouyer, F., Simmler, M.-C., Johnsson, C., Vergnaud, G., Cooke, H.J. & Weissenbach, J.A. (1986) A gradient of sex linkage in the pseudoautosomal region of the sex chromosomes. *Nature*, **319**, 291–5.

Sargent, C.A., Boucher, C.A., Blanco, P. *et al.* (2001) Characterization of the human Xq21.3/Yp11 homology block and conservation of organization in primates. *Genomics*, **73**, 77–85.

Sargent, C.A., Briggs, H., Chalmers, I.J., Lambson, B., Walker, E. & Affara, N.A. (1996) The sequence organization of Yp/proximal Xq homologous regions of the human sex chromosomes is highly conserved. *Genomics*, **32**, 200–9.

Schwartz, A., Chan, D.C., Brown, L.G., Alagappan, R., Pettay, D., Disteche, C., McGillivray, B., de la Chapelle, A. & Page, D.C. (1998) Reconstructing hominid Y evolution: X-homologous block, created by X–Y transposition, was disrupted by Yp inversion through LINE–LINE recombination. *Human Molecular Genetics*, **7**, 1–11.

Stringer, C. & McKie, R. (1996) *African Exodus: The Origins of Modern Humanity*. London: J. Cape.

Turner, A. (1994) The species in palaeontology. In: *Speciation and the Recognition Concept: Theory and Application* (eds D. M. Lambert & H. G. Spencer), pp. 57–70. Baltimore: Johns Hopkins University.

Turner, G.F. & Burrows, M.T. (1995) A model of sympatric speciation by sexual selection. *Proceedings of the Royal Society of London B*, **260**, 287–92.

West-Eberhard, M.J. (1983) Sexual selection, social competition and speciation. *Quarterly Review of Biology*, **58**, 155–83.

Whittington, J.E. & Richards, P.N. (1991) Mathematical ability and the right-shift theory of handedness. *Neuropsychologia*, **29**, 1075–82.

Zangwill, O.L. (1960) *Cerebral Dominance and its Relation to Psychological Function*. Edinburgh: Oliver & Boyd.

Zink, R.M. (1996) Species concepts, speciation, and sexual selection. *Journal of Avian Biology*, **27**, 1–6.