

Finger-length ratios and sexual orientation

Measuring people's finger patterns may reveal some surprising information.

Animal models have indicated that androgenic steroids acting before birth might influence the sexual orientation of adult humans. Here we examine the androgen-sensitive pattern of finger lengths¹, and find evidence that homosexual women are exposed to more prenatal androgen than heterosexual women are; also, men with more than one older brother, who are more likely than first-born males to be homosexual in adulthood², are exposed to more prenatal androgen than eldest sons. Prenatal androgens may therefore influence adult human sexual orientation in both sexes, and a mother's body appears to 'remember' previously carried sons, altering the fetal development of subsequent sons and increasing the likelihood of homosexuality in adulthood.

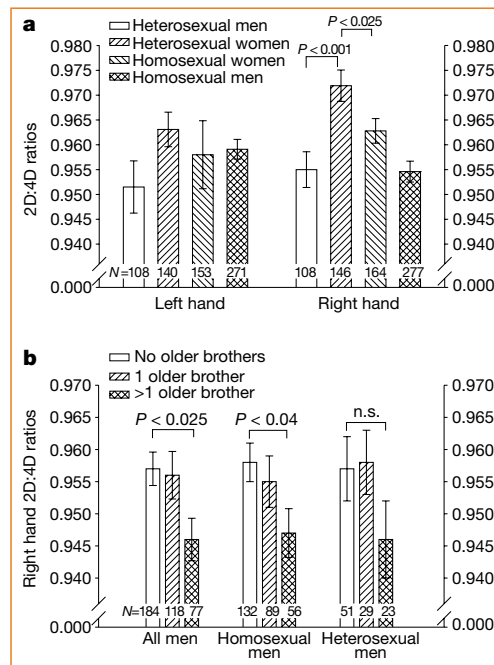
In women, the index finger (2D, second digit) is almost the same length as the fourth digit (4D), although it may be slightly longer or shorter; in men, the index finger is more often shorter than the fourth. The greater 2D:4D ratio in females is established in two-year-olds¹. Because all non-gonadal somatic sex differences in humans appear to be the result of fetal androgens that masculinize males³, the sex difference in the 2D:4D ratio probably reflects the prenatal influence of androgen on males⁴.

In an anonymous survey, 720 adults who were attending public street fairs in the San Francisco area were asked their gender, age, sexual orientation, handedness, and the number and gender of children their mother had carried before them. As expected, men have significantly longer fingers than women ($P < 0.001$), and we confirmed reports that the 2D:4D ratio is greater in women than it is in men.

This sex difference in 2D:4D is greater on the right hand than on the left (Fig. 1a), indicating that the right-hand 2D:4D is more sensitive to fetal androgens than the left-hand ratio. The right-hand 2D:4D ratio of homosexual women was significantly more masculine (that is, smaller) than that of heterosexual women, and did not differ significantly from that of heterosexual men. Thus finger ratios, like otoacoustic emissions⁵, suggest that at least some homosexual women were exposed to greater levels of fetal androgen than heterosexual women.

The 2D:4D ratio of homosexual men was not significantly different from that of heterosexual men for either hand ($P > 0.09$). However, segregating male subjects based on birth order provided support for the role of fetal androgens in male sexual orientation. The more older brothers a boy

Figure 1 Finger-length patterns vary with gender, sexual orientation and birth order. **a**, Among heterosexuals, the mean 2D:4D ratio is larger in women than in men, especially on the right hand. The right-hand 2D:4D ratio of homosexual women is more masculine (that is, smaller) than that of heterosexual women. **b**, Men with more than one older brother are more likely to be homosexual² and have a significantly more masculine right-hand 2D:4D ratio than men without older brothers. Subjects were offered lottery 'scratcher' tickets for their participation. Age and handedness were not significantly different between heterosexual and homosexual subjects; we found no relation between handedness or age and finger measures. Finger lengths were measured blindly from photocopies of subjects' hands. Repeated measurements from 381 subjects were highly correlated ($r = +0.95$ to $+0.99$). Standard errors of the means are depicted. All P values, from Student's t -tests, are two-tailed. n.s., Not significant.



has, the more likely he is to develop a homosexual orientation². Confirming these reports, we also found that only homosexual men had a greater than expected proportion of brothers ($P < 0.01$) among their older siblings (229 brothers: 163 sisters) compared with the general population (106 males: 100 females⁶).

We found that the male 2D:4D ratio, which is unlikely to be influenced by social factors, also varies with the number of older brothers. The ratio was significantly more masculine in men with two or more older brothers than in men with no older brothers (Fig. 1b). There is also a significant correlation ($r = -0.104$; $P < 0.05$) between the number of older brothers and the right-hand 2D:4D ratio in men. If male subjects are divided by sexual orientation, the same pattern of later-born men displaying a more masculine 2D:4D is seen. Having older sisters has no apparent influence on male sexual orientation², or on the 2D:4D ratio in men. No effect of older brothers or sisters on 2D:4D in women was observed, consonant with reports that older siblings exert no effect on female sexual orientation⁷.

Our results suggest that events before birth (or even before conception in the case of older brothers) influence human sexual orientation. The masculinized right-hand 2D:4D ratio in homosexual women may reflect fetal androgen levels that are slightly higher than in heterosexual women. Homosexual men without older brothers have 2D:4D ratios indistinguishable from hetero-

sexual eldest sons, indicating that factors other than fetal androgen (such as genetic influences^{8,9}) also contribute to sexual orientation. Finger measures indicate that men with more elder brothers, including those men who develop a homosexual orientation, might be exposed to greater than normal levels of prenatal androgen.

Although hyper-androgenization of homosexual men might not fit some cultural expectations¹⁰, homosexual men display several hyper-masculine characteristics, including a greater mean number of sexual partners in a lifetime than heterosexual men, who in turn report more sexual partners than do women of either orientation. Furthermore, reports that adult homosexual men have more circulating androgens (ref. 11, but see ref. 12), larger genitalia¹³ and more 'masculine' auditory evoked potentials than heterosexual men¹⁴, are consistent with at least some homosexual men being hyper-androgenized.

Although it is possible that the maternal influence on finger growth of subsequent sons occurs after birth, a prenatal influence seems more likely because of the extensive physiological pairing of mother and fetus. The locus of the maternal 'memory' for previous sons, and the mechanisms by which fetal development of subsequent sons is altered, remain unknown.

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Drosophila cryptochromes

A unique circadian-rhythm photoreceptor

Cryptochrome proteins are critical for circadian rhythms, but their function(s) is uncertain. Here we show that a mutation in a cryptochrome (dCRY) from the fruitfly *Drosophila* blocks an essential photoresponse of circadian rhythms, namely arrhythmicity under constant light conditions. We conclude that dCRY acts as a key photoreceptor for circadian rhythms and that there is probably no other comparable photoreceptor in this species.

Constant light causes the intrinsic circadian period of diurnal animals to shorten and that of nocturnal animals to lengthen (Aschoff's rule). More intense light produces more extreme effects, ultimately resulting in arrhythmicity¹ in most mammals and birds. The circadian period of arthropods generally lengthens in constant light, whether the animal is nocturnal or diurnal¹. *Drosophila melanogaster* is no exception and intense constant illumination leads to arrhythmicity².

The cryptochrome family includes blue-light photoreceptors³. The single known *Drosophila* cryptochrome is thought to be a circadian photoreceptor: flies carrying a mutant allele, *cry^b*, have severely decreased circadian photoresponses⁴, whereas overproduction of dCRY causes increased photosensitivity⁵. In mammals, however, mCRY1 and mCRY2 are more likely to be involved in the central clock mechanism^{6–8}.

This raises the possibility that dCRY effects on photosensitivity reflect a role downstream of circadian photoreception, somewhere along the circadian light-input pathway or within the *Drosophila* central clock itself. This fits with the fact that *cry^b* flies are still able to reset their circadian rhythm (entrain) to new light–dark cycles². We find, however, that *cry^b* flies remain behaviourally rhythmic in intense constant light, in contrast to wild-type flies and many other species which are arrhythmic under such conditions (Fig. 1a,b)^{1,2}.

The arrhythmicity of *cry^b* flies must be a

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property of the *cry* gene, because the normal phenotype can be rescued by expressing wild-type dCRY in rhythm-generating cells of *cry^b* flies. In intense constant light, the *cry^b* mutant's behaviour is strikingly similar to that of wild-type flies in constant darkness (Fig. 1c). An identical 24.7-hour period is also recorded under constant-darkness conditions, indicating that this slightly longer period is a characteristic of the background genotype. Thus, there is not even a detectable lengthening of period in the *cry^b* mutant strain under constant light condi-

tions². The free-running, circadian nature of *cry^b* flies' constant-light behaviour is further demonstrated by the 19.2-h period observed for flies with *cry^b* in combination with a short allele of the *period* gene (*per^s*; Fig. 1a).

Our results show that the *cry^b* mutation impairs the circadian photoreception pathway so profoundly that the fly cannot 'see' constant light. This mutant also responds very poorly to short light pulses⁴; by these criteria, this circadian photoreceptor must be unique in *Drosophila*. How then can *cry^b* flies entrain to different 24-h light–dark cycles? The missense *cry^b* mutation might generate a protein with weak activity that would be sufficient for light–dark entrainment but not for a normal arrhythmic behavioural response to constant illumination. However, our previous results suggest a different explanation: entrainment of *cry^b* flies is through a second, completely separate light-input pathway⁴. Visual photoreception^{4,9} may even directly influence locomotor activity, which then affects circadian rhythms only indirectly through a non-photoc phase-resetting pathway.

Our results indicate that dCRY is an important circadian photoreceptor and

Figure 1 *cry^b* circadian rhythms free-run under intense constant light. **a**, *cry^b* behavioural rhythmicity and rescue of wild-type arrhythmicity. Flies were entrained under a normal 12-h light:12-h dark regime for 3 d. At the end of the fourth light period, the light was left on at saturating light intensities (2,000 lux) and activity monitored over the next 6 d. The last 5 d were used to analyse locomotor activity rhythms. *tim-GAL4* and *UAS-cry* are two transgenes⁵ used to express wild-type CRY in circadian-rhythm-generating cells of *cry^b* flies. *N*, number of flies analysed; % AR, percentage of arrhythmic flies (cut off, 'power' <10 or 'width' <2; ref. 10); τ , period length of the circadian behavioural rhythms in hours. Value in parentheses is based on only two weakly rhythmic flies. **b**, Representative *y w* and *y w;cry^b* actograms; data are double-plotted. After the light is permanently left on (arrow), *cry^b* fly behaviour starts to free-run, whereas wild-type flies become arrhythmic. The first day of entrainment is not shown. White boxes, days or subjective days; black boxes, nights or subjective nights. **c**, Average activity plots of 14 *y w* and 16 *y w;cry^b* flies under constant light conditions (LL), and 16 *y w* flies under light–dark (LD) or constant-darkness conditions (DD). White bars, days or subjective days (zeitgeber or circadian time, 0–12); black bars, nights or subjective nights (zeitgeber or circadian time, 12–24). Each bar represents the 5-day average activity of a pool of flies during a specific 30-min period of the day (for example, the first white bar of an LD plot is the average activity of a pool of flies between zeitgeber time 0 and 0.5 during the 5 d of measurement). Dots, standard deviation.

