

Note

**1927 Study Supports a Current Genetic Model for Inheritance of Human Scalp
Hair-Whorl Orientation and Hand-Use Preference Traits**

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Running Head: Genetics of human scalp hair-whorl rotation

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ABSTRACT

The cause of right versus left hand-use preference in humans has been debated for a long time. Culturally learned, birth stress, and biologically specified causes are the prominent etiologies under consideration. A 2003 (KLAR 2003) study reported a correlation between the person's preferred hand and the scalp hair-whorl orientation developed on the head. By reinterpreting results of a 1927 (SCHWARZBURG 1927) study on genetics of the hair-whorl trait, support to a recent single gene, two alleles "random-recessive model" for both hair-whorl orientation and handedness traits inheritance is demonstrated.

Most persons prefer to use their right hand (referred here as RH) for one-handed tasks, such as writing, throwing a ball, hammering, sawing, cutting with a knife, and so on, but a significant minority prefers to use the left (LH) or either hand (ambidextrous). The term NRH (for non-right hander) will be used here to represent both left- and ambidextrous-hand users. The question of whether hand-use preference, referred to as handedness, is specified by biology/genetics, by cultural training, by pathological reasons such as birth stress, or by a combination of these etiologies has been addressed for decades and the debate continues. Several observations suggest problems with a strict genetic etiology. For example, not all the children of RH X RH are RH; not all the children of NRH X NRH are NRH; 18% monozygotic twins are discordant for handedness even though co-twins possess identical genetic makeup; cultural pressures can change some persons' preference (RIFE 1940). A relatively recent "random-recessive model" postulated first, that a single hypothetical gene named *RGHT1* (for specifying right handedness) is fully penetrant causing persons with one or two *RGHT1* copies to become RH, second, that the recessive non-functional allele *r/r* (*r* for random) homozygous persons develop as a fifty-fifty mixture of RH and NRH and third, that monozygotic twins discordance results from randomness due to their *r/r* genotype (KLAR 1996).

For etiology determination, one of the best definitions of handedness was proposed by Rife (RIFE 1940). This rather strict definition designates a person as RH if the right hand is preferentially used for *all* 10 tasks such as to throw a ball, use a spoon, saw, sew, shoot marbles, bowl, cut with a knife, cut with scissors, hammer, and to write. NRH are defined those who do any number of these tasks with their left or with either hand. Following this definition, the random-recessive model was supported by several findings: the value of 7.6% NRH children born to RH X RH parents (RIFE 1940) is as predicted (KLAR 1996); a three-generational study suggested that the RH progeny of a LH X LH cross possess the *r/r* genotype (KLAR 1996); the study of discordant twin's progeny suggested twins to possess the *r/r* constitution (KLAR 2003). Furthermore, a recent study noted an interesting association of handedness with the direction of parietal (scalp) hair-whorl rotation found

on the top of the human head (Figure 1). Specifically, it was discovered that NRH comprise of a random mixture of clockwise (C) and counter-clockwise (CC) persons, and also, persons chosen for their CC orientation were evenly divided between RH and NRH. In contrast, most people (over 90%) in the general public are RH and most persons (over 90%) support a C hair-whorl rotation. Based on such partial association in seemingly unrelated traits, it was suggested that both handedness and hair-whorl orientation are controlled by two alleles of a single gene. Individuals containing the *RGHT1* allele are RH and develop C hair whorls and in *r/r* individuals there is no association between the traits and they are randomly distributed to the left versus right side of a person (KLAR 2003). However, conclusions of the hair-whorl study were challenged in a recent commentary. Instead, in the commentary it was suggested that most NRH result from a combination of causes, mostly from damage to the language-processing left brain hemisphere owing to birth stress (“pathological left-handers”), and a minority from learned reasons (“learned left-handers”), and the authors speculated that at most less than 20% of NRH may be genetically determined (EHRMAN and PERELLE 2004).

A major problem faced in studies of a “complex trait,” such as handedness, concerns the criteria used to define a person’s handedness. It is likely that by varying the definition of a complex trait or the population ethnicity under study, results of different studies could significantly vary making it difficult to compare conclusions of one study with those of others. Fortunately, a common human trait exists which is immune to subjective errors in scoring phenotype. In over 95% of humans each person supports a single hair whorl on the scalp, the rest have two whorls each (Figure 1), and more than two whorls are extremely rare. Also, the whorl orientation does not change with aging or by the direction hair is combed. Of equal importance, the phenotype is not subject to cultural influences or to birth stress. Thus, the hair-whorl orientation is a much more definitive phenotype as compared with handedness, and it should be exploited for deciphering the etiology of handedness in the general public. Therefore, to scrutinize the genetic interpretation for partial correlation between the traits of handedness and hair-whorl orientation proposed in the random-recessive model (KLAR 2003), and to address the validity of the birth stress etiology (EHRMAN and PERELLE 2004), family studies concerning inheritance of the hair-whorl trait would be very informative for deciphering the handedness etiology of the

general public. Fortunately, such an extensive and highly informative study was published long ago in 1927!

The most telling result concerns study of inheritance of the hair-whorl trait in nuclear families (SCHWARZBURG 1927). The single gene, two alleles model was advanced whereby individuals containing one or two copies of the dominant allele (designated *R*) develop C whorls and *all* the recessive non-functional *r/r* allele homozygous persons develop CC type (Schwarzburg model, Figure 2). The study concluded that a single gene controls hair-whorl orientation, clockwise as a dominant trait, individual's sex does not influence orientation, and that whorl orientation is not linked to the eye color. According to the model, the frequency of 0.286 CC progeny found in C X CC families suggested 0.286 *r* : 0.714 *R* allele ratios in C parents. According to thus derived allele frequency, C X C families should produce $0.286 \times 0.286 = 0.081$ fraction of children supporting CC orientation. However, the predicted 0.081 value differed significantly from the observed 0.158 value ($\chi^2 = 6.45$, d. f. =1, $p < 0.05$), a result that contradicted the model (Figure 2). We propose that the contradiction derives from an incorrect feature of the model that required all *r/r* individuals to develop CC orientation.

According to the random-recessive model, however, *r/r* individuals should exhibit 50% C : 50% CC whorl orientation ratio (KLAR 2003). Consequently, the frequency of 0.286 CC children born to C X CC parents predicts $0.286 \times 2 = 0.572$ fraction of the progeny should possess the *r/r* genotype. Therefore, their C parents should harbor 0.572 *r* : 0.428 *RGHT1* allele frequencies. According to this allele frequency, the C X C families are predicted to produce $0.572 \times 0.572 \times 50\%$ (50% for the randomness parameter of the random-recessive model) = 0.163 CC progeny frequency (Figure 2). The predicted value is remarkably similar to the observed value of 0.158 ($\chi^2 = 0.01$, d. f. =1, $p > 0.90$). There was only one family reported in the study concerning CC X CC cross where all 3 children exhibited CC orientation (Figure 2). The small number of three persons is statistically too small to differentiate between the models under consideration, and the result is not statistically inconsistent with the random-whorl orientation expectation of the random-recessive model.

A recent study (KLAR 2003) suggested that *RGHT1* gene functions for brain hemisphere left-right laterality development so that the left-brain hemisphere processes language, and

that the gene functions to couple the dominant hemisphere to the development of both right-hand preference and clockwise hair-whorl rotation. It follows that *r/r* individuals develop these traits but at least the traits of handedness and hair-whorl rotation are randomly distributed with respect to each other and to the left-right axis of a person [reviewed in (KLAR 2004a)]. The etiology of handedness continues to be debated despite hundreds of studies conducted over many decades. The hair-whorl study was performed a long time ago. By advancing an alternate explanation to the results, rediscovery and significance of the study to decipher the handedness etiology is recognized here. Ironically, and from a historical perspective, it is noteworthy that the hair-whorl trait was one of a handful of very early human traits exploited to study genetics in humans; the others being eye color, blood groups, the M and N agglutinogens, presence of hair on the second joint of the digits, and the taste deficiency. The 1927 hair-whorl study provides support to the random-recessive model originally advanced to explain the etiology of handedness. Here I conclude that the same genetic mechanism explains the inheritance of the hair-whorl phenotype in the general German population. Thus the suggestion that handedness and hair-whorl traits develop from variation in a single gene/two alleles hypothesis (KLAR 2003) is supported by the 1927 study. As the non-alterable whorl orientation is established prior to birth, the finding of association between handedness and the hair-whorl traits, combined with other similar arguments (KLAR 2004d), the results argue against birth stress or other learning based etiologies (EHRMAN and PERELLE 2004) for handedness in the general public.

A very significant variation in the handedness allele frequency is noteworthy in these two studies. In single-whorled persons only 8.4% ($n = 500$) were reported to be CC in the United States population (KLAR 2003), while nearly 20% ($n = 3960$) exhibited CC rotation in the German population (SCHWARZBURG 1927). The *r* allele frequency derived by Schwarzburg should be doubled according to the random-recessive model. This difference suggests a significant variation in the allele frequencies of the two populations, results of which were recorded over seven decades apart. Further studies are needed to quantify variations in the handedness allele frequencies in other geographical regions, ethnic populations, and even people from different professions by exploiting the easily discernable hair-whorl phenotype. It should be noted in this context that LH is rare

among African children (VERHAEGEN and NTUMBA 1964), while the United States Jewish college-students were reported to be twice as likely to be NRH compared to the Gentile population (RIFE and SCHONFELD 1944). In addition, the hair-whorl phenotype may be exploited to study the contribution of genetics concerning development of brain hemispheric laterality to other human behaviors, including a persons` life style. For example, it was recently reported that homosexual men enriched samples exhibit a 3.6-fold excess of CC orientation as compared to men at large in the United States population (KLAR 2004b). With overwhelming experimental support garnished for genetic etiology, researchers should next address what biological function the *RGHT1* gene performs to influence left-right laterality development of neuronal tissues influencing brain laterality, handedness, and hair-whorl orientation. At present only a single suggestion has been made in this context. On the basis of strictly genetic results, it was recently suggested that the *RGHT1* facilitates patterned segregation of chromosome 11 chains in mitosis to differentiate sister cells at a specific cell division in embryogenesis ultimately leading to brain hemispheric specialization (KLAR 2002; KLAR 2004c).

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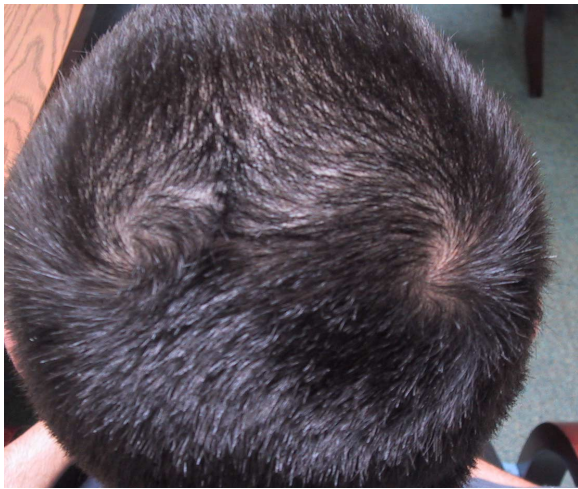


Figure 1. The parietal hair-whorl phenotype. Most persons have a single hair whorl (top) and the minority exhibits two whorls (bottom). Among those with single whorls, the minority exhibits counter-clockwise (top) rotation and the majority develops the clockwise orientation (not shown). Thus, the majority of people have a single clockwise hair whorl (KLAR 2003).

A. Crosses		
$C^* \times CC$	$C \times C$	$CC \times CC$
↓	↓	↓
CC progeny: 0.286 (n = 49)	0.158 (n = 82)	3 persons

B. Predictions		
Model	C^* <i>r</i> -allele frequency	CC progeny fraction of the $C \times C$ cross
Schwarzburg model (all <i>r/r</i> are CC)	0.286	0.081 (0.286 x 0.286)
Random-recessive model (<i>r/r</i> are 50% C : 50% CC)	0.572 (0.286 X 2)	0.163 (0.572 X 0.572 X 50%)

Figure 2. Results (SCHWARZBURG 1927) of hair-whorl trait inheritance from nuclear families are presented in A. The calculated *r*-allele frequencies of the starred C parent of the $C \times CC$ cross, and thereby predicted frequencies of CC progeny from the $C \times C$ cross are presented for both models in B. The data satisfy a key prediction of the random-recessive model for inheritance of hair-whorl and the handedness traits. C = clockwise, CC = counter-clockwise.

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