

**The Right Shift Theory of Handedness and Brain Asymmetry in Evolution,
Development and Psychopathology.**

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Abstract

The right shift (RS) theory suggests that lateral asymmetries arise from accidental differences between the sides of the body. There is an additional specific influence on human brain asymmetry, an RS + gene present in some but not all people, that induces advantage for the left hemisphere by weakening the right hemisphere. The theory explains associations between handedness and cerebral specialisation for speech, and also handedness in families and twin pairs. The gene is expected to be specific to *Homo sapiens*. It is expressed through processes that influence brain development and it is hindered by factors that impair normal growth processes. Most raised incidences of nonright-handedness in pathological conditions are secondary to processes that disrupt growth. It is possible, however, that the RS + gene is unstable and mutates to a form which is agnostic for left versus right. This could result in the impairment of speech and language skills in both hemispheres, a possible cause of schizophrenia and perhaps also autism. The effects of the RS + gene on human handedness and other asymmetries often appear weak because they must be detected against the background noise of chance. The RS + gene induces typical cerebral specialisations in most of the population but in its' absence there are risks to the efficiency of speech and phonological processing. Questions about costs and benefits associated with the RS locus deserve further research.

The essential features of the right shift (RS) theory of handedness and cerebral specialisation were formulated by Annett (1972), but the implications of these ideas have been explored in stages over some 30 years, leading to several new developments. The current theory is summarised here but there is not space to describe the empirical studies on which it is based. Readers are referred to Annett (2002) and subsequent publications for details. For comparisons with other theories of handedness see also Annett (2002). Critical reviews of Annett (2002) were published by Corballis (2004), Crow (2004), Elias (2004) and McManus (2004), together with author's response (Annett, 2004). This review considers the relevance of the RS theory to questions about evolution, development and psychopathology, and describes new work in each of these areas.

The Right Shift Theory

Figure 1

Figure 1 gives a schematic overview of the main elements of the RS theory of handedness and cerebral specialisation. Level 1 represents chance, the main and universal agent of asymmetry, as a pin ball machine. It must be imagined that small balls are dropped through the funnel at the top and bounce off the pins as they fall. The progress of each ball represents the process of early growth in the individual, buffeted by accidents of development. The normal curve is intended to show the distribution that would occur, on average, for many individuals. The baseline represents differences in efficiency between the two sides of the body that would arise from random influences on either side during development. The genetic instructions may be identical for the two sides, but differences arise as the instructions are translated in muscles, nerves, blood supply, and other characteristics of functioning

organs. As in the construction of any bilaterally symmetrical object (a model toy, a jacket, a building) one side may be put together better than the other. For most people, those in the centre of the distribution, there are no noticeable differences between the sides but at the extremes there might be large asymmetries. Chance differences of this kind are sometimes referred to as 'fluctuating asymmetry'.

The second element of the theory is an RS+ gene that induces left cerebral hemisphere advantage, represented as small bars that deflect the initial trajectory of the balls. The deflection changes the location but not the shape of the distribution. The normal curves are displaced a short distance to the right by a single bar, and further by two bars. That is, the effect of the gene on physical asymmetries of hand and brain is expected to be additive. Some humans do not carry the gene. In RS - - genotypes the normal distribution remains unbiased to either side, with a mean difference between the sides at zero and independent lateralisations of speech and handedness. That is, there is no intrinsic connection between speech laterality and handedness.

Level 3 shows the three genotypes, RS - -, RS + -, RS + +, with means at about zero and one and two standard deviations (0z, 1z, and 2z respectively). The letter 'x' represents the threshold for left-handed writing at about 10% of the population. Notice that the majority of RS - - genotypes are to the right of the threshold. Social pressures persuade most people with equal skill in both hands to use the right hand for writing and other socially salient actions such as eating. The overlap of the distributions shows that many gene carriers are to the left of 'x'. The gene does not determine right-handedness directly, but merely increases the probability of superior skill on the right side. The directional shift is added to the accidents of early development, like a weighting factor added to a chance throw. The model for

handedness is chance **and** RS (present or absent). However, the functional effect of the presence of the RS + gene is expected to be lateralisation of speech to the left hemisphere. For cerebral speech the model implies directional bias *or* chance (as in the model of Layton, 1976, for situs inversus of the viscera). However, the physical bases of asymmetries for both brain and hand are expected to be continuous normal distributions (with or without RS).

Level 4 represents the extent of shift, or the effect of the RS + gene in displacing the chance distribution to the right. Gene expression depends on growth processes that vary with factors such as sex, twinning and low birth weight. Shifts are estimated to be normally about 1.0z per gene for males and 1.2z for females. These estimates are reduced by about 33% in twins.

The fifth element of the model is the cut-points, or thresholds, along the baseline of asymmetries between the hands in skill, that are associated with various expressions of hand preference. Thresholds are expected to vary with cultural pressures, as outlined above. Toward the left extreme are people who perform all skilled actions with the left hand (consistent left-handers). Less far to the left are people who write with the left hand, but perform other skilled actions such as throwing, or cutting with scissors with the right hand. Further to the right are people who write with the right hand but prefer the left hand for some other skilled action (nonright-handers). The frequencies of these three levels of hand preference are about 3-4%, 9-10% and 35-40% respectively, in modern western societies. One of the most difficult problems for evaluation of the handedness literature is that researchers apply the term 'left-hander' at many different cut-points along the continuum.

The RS model makes a clear distinction between the shape of the distribution (the normal curve) and the location of the distribution (displaced to the right). The shape of the distribution is expected to be common to all animals with bilaterally symmetrical limbs but the RS displacement is expected to be unique to humans. Left versus right paw preferences in mice are clear in individuals, distributed as expected by chance in each generation, and not inherited between generations (Collins, 1969). For humans, there appears to be a genetic influence, superimposed on the chance background. The interesting question about human handedness is what causes RS and the obvious first hypothesis must be that it is something that gives an advantage to the left hemisphere, weighting the chance probabilities in favour of the right hand. The assumption that RS was a factor for left hemisphere speech led to an analysis of the literature on dysphasia following right or left brain damage. The model is consistent with findings for handedness and speech laterality in dysphasics with left or right hemisphere lesions (Annett, 1975; Annett & Alexander, 1996) and also in normal samples (Knecht et al., 2000).

Application of the model to the problem of the inheritance of handedness showed that a single gene could account for handedness in families (Annett, 1978, 1999a, 2003). The gene and genotype frequencies were not derived from the family data itself, but from the proportion of right hemisphere speakers in samples of dysphasics drawn from the general population. This supports the argument that it is a gene for left hemisphere speech lateralisation that displaces the handedness distribution to the right. Further support for the genetic analysis was found when it was discovered that associations between lateral asymmetries, such as handedness and

eyedness or footedness, or writing and throwing, were predictable if each was influenced by the RS + gene independently and combined at random (Annett, 2000).

The genotype distributions (level 3 of Figure 1) show that the most frequent is the heterozygote (RS + - genotype at about 49.0%) while both homozygotes (RS - - at about 18.5% and RS ++ at about 32.5%) are smaller. This raises the possibility that there is a genetic balanced polymorphism with heterozygote advantage for the RS locus (Annett, 1978). What are the relative advantages and disadvantages of the presence versus absence of the RS + gene? This question has been researched in many studies. An important finding was that strong right-handedness is associated with weakness of the left hand rather than added skill in the right hand. This raises the possibility that RS + induces left hemisphere advantage by weakening the right hemisphere and perhaps its associated physical and cognitive skills.

The Evolution of Lateral Asymmetries

The RS hypothesis originated in a comparison of distributions in humans and other species. Numerous studies of hand and paw preferences have found that nonhumans may have strong preferences as individuals but that left and right preferences are about equal, the majority not strongly biased to either side. There is no evidence of species bias to either side in mice (Collins, 1969), monkeys (Lehman, 1978; Warren, 1953) or chimpanzees (Finch, 1941). (Claims to the contrary are discussed below.)

When animals are classified as strongly left or right preferent (some 80-90% consistent use of one side) the proportions of left-, mixed- and right-handers are about 25%, 50% and 25% respectively. When humans are classified as consistently right or left preferent for all items of the 12 item Annett Hand Preference Questionnaire (Annett, 1970) there are about 4%, 33% 63% left-, mixed- and right-handers. If these

percentages are looked up in the table of the normal curve to find the thresholds which distinguish strong left-handers from mixed-handers (TL) and strong right-handers from mixed-handers (TR), it will be found that the distance between TL and TR is the same for humans and nonhumans. The distributions can be superimposed, the nonhuman distribution centred at 0z, and the overall human distribution mean at just over 1z. This was the surprising discovery that suggested that the distributions are identical except for human RS. The implication for evolution is that asymmetries occur in several species, but humans are unique in having RS for handedness.

There are many asymmetries in nature (review by Bradshaw and Rogers, 1993) that tempt speculations as to possible continuities of asymmetries by descent. For example, Corballis (2003) argued for links between species with vocalisations that appear to depend on left brain structures, bias to right-handedness, an early gestural language for human communication, and modern speech gestures. There are intimate associations between cerebral motor areas for the hand and speaking, reading and listening to speech, but these associations occur in both hemispheres and are not lateralised (Breitenstein, Floel, Drager & Knecht, 2003). Other commentaries on Corballis's target article were published with the 2003 paper.

Some song-birds depend on the left side of the brain more than the right for key elements of song (Nottebohm, 1970). There appear to be asymmetries in the skulls of whales (Ness, 1967) that may relate to their ability to transmit sounds over long distances. These asymmetries suggest there are advantages for the control of complex vocal output from one side of the brain. However, this does not imply direct descent from birds or whales to man. The number of species for which lateralised vocalisations or limb use are *absent* is more impressive than those in which they are

present. In my view, the evidence suggests that asymmetries evolved several times independently to meet particular needs, without necessary continuity. The critical questions for direct descent in humans depend on lateralities in chimpanzees and other higher primates. Chimpanzees make a variety of vocalisations but nothing resembling human speech. Attempts to teach chimpanzees to speak have found this impossible. Chimpanzees can communicate by other means, such as sign language and symbols on computer keyboards. They may have rudimentary forms of language, but they do not have speech (Fouts & Mills, 1998; Taglialatela, Savage-Rumbaugh & Baker, 2003).

The distinction between speech and language was shown to be important in human brain damaged children. Annett (1973) found that children with right and left hemiplegias and equivalent levels of disability on the two sides (as measured by the Annett peg moving task) were virtually identical for levels of intelligence, both verbal and nonverbal. However, children with early *left* brain damage had a history of difficulties in the development of speech more often than right brain damaged children, usually resolved at the time of testing. Hence, it is suggested that the RS + gene is something that facilitates early speech acquisition. It is not a gene 'for' speech or language in general. The typical pattern of hemisphere specialisations for language and other functions would be likely to follow from an initial bias to the left side for speech, but there may be no necessary dependence on the left hemisphere for speech or language. The advantage of lateralisation of speech to one side of the brain is probably to reduce the need to transmit signals between the hemispheres. Inter-hemispheric communication might be particularly difficult for a large brain when controlling the subtle gestures of mouth and vocal tract needed for speech.

Evidence for anatomical asymmetries in the skulls of hominids (Holloway, 1995; Steele, 2000; Tobias, 1995) suggests that the RS + gene may have arisen early in human evolution. The evolution of speech probably took several millennia. The stages needed to progress from first words like those of a 1-2 year old to an ability to manipulate the propositions of symbolic logic could well have taken all the time from the first hominids to modern humans.

Could RS have arisen even earlier? McNeilage, Studdert-Kennedy and Lindblom (1987) argued that some species of monkey are biased to the left hand and some higher primates biased to the right but Annett (1987b) found the supposed evidence weak. Most accounts of hand preferences in chimpanzees report no systematic bias to either side (Fletcher & Weghorst, 2005; McGrew & Marchant, 1997; Papademetriou, Sheli & Michel, 2005). If some primates were found to have lateral biases would the RS argument be invalidated? I think not because it would still apply to all the other species of primates for whom specific biases have not been claimed. The so-called exceptions would then require special scrutiny.

Gannon, Holloway, Broadfield and Braun (1998) found chimpanzees to have brain asymmetry of the planum temporale, larger on the left side in 94% of brain specimens they examined. As leftward asymmetries of this area have been associated with speech processing in humans, the question arises what this region is for, if not speech. However, further analysis of the micro-anatomy of the planum temporale found that asymmetries that are normally present in human brains are absent in chimpanzees (Buxhoeveden, Switala, Litaker, Roy, & Casanova, 2001).

Hopkins has reported for some years that chimpanzees resemble humans for several lateral asymmetries. Hopkins et al. (2005) summarised data for 180

chimpanzees performing a bimanual task, retrieving peanut butter smeared inside a hollow poly-vinyl-chloride tube. The animals were classified as left or right preferent using a fairly strong criterion, and others were called 'ambiguous' handed ('mixed' on my terminology). There were 17% left-, 46% mixed- and 37% right-handed animals. The proportion of right-handers was significantly greater than that of left-handers. This was the basis of Hopkins' claim that chimpanzees are right-handed. However, it is evident that only about one-third of the animals were right preferent and two-thirds were nonright-handed.

The distribution of most non-humans was shown above to be about 25% left-, 50% mixed- and 25% right-handers. There were fewer left- and more right-handed animals than expected for this chance distribution in Hopkins' sample. Can we say that chimpanzees are shifted to the right? Annett (2006) showed how to estimate the extent of RS by taking the midpoint between the thresholds (TL and TR) when the proportions of animals to the left of each threshold are expressed as z values under the normal distribution function. RS can be calculated as $(TL + (.5(TR-TL)))$. On this calculation, Hopkins' chimpanzees were biased to the right by about 0.3z. Hopkins et al. (2005) described data for 4 samples using less strong preference criteria. Estimates of shift in all cases were about 0.3z. If there is a reliable shift to the right in the handedness of chimpanzees it is small in comparison with the overall distribution for humans (about 1.0z). If RS was present in the common ancestor of humans and chimpanzees it has either become greatly reduced in chimpanzees or greatly expanded in humans. However, before speculating along these lines it is essential to have strong and independent replications of Hopkins' findings.

The Development of Handedness and Brain Asymmetry.

The development of living organisms depends on processes in which genetic instructions are realised in the environment. This entails multiple interactions between genetic and environmental constraints which lead to particular phenotypic outcomes. In this most general sense it must be true, but also trivial, that outcomes for laterality and cerebral dominance depend on developmental processes. Can we be more specific with respect to the RS theory? At what stages of development do critical influences operate on lateral asymmetries? Do these asymmetries influence the functional efficiency of skills such as speaking and reading?

The schematic representation of the RS theory in Figure 1 suggests two main ways in which developmental processes influence outcome. First, the chance fall of balls in the pin-ball machine is envisaged as a series of accidents of development, as outlined above. The second main developmental variable is the extent of shift. The shift depends on a genetic influence, but one that has to be expressed through growth in the individual. When growth rates differ, as between the sexes and between twins and the singleborn, or in low birth weight infants, gene expression may be restricted and hence RS reduced.

Girls are slightly more mature at birth than boys, and they maintain this faster growth trajectory until puberty (Tanner, 1978). Girls are also a little more likely to be right-handed than boys, although the difference is so small that large samples are needed to detect it. On the Annett peg board test of hand skill girls have a significantly greater bias in favour of the right hand than boys. The growth of twins must be slowed in order to accommodate two foetuses in the womb. Twins are less likely to be right-handed than the singleborn. Annett (1987a) found on a square marking test, in a large national survey of 11 year old children, that bias to the right

hand was strongest in singleborn females and weakest in twin born males, with singleborn males and twin females intermediate.

The question whether twins are more often left-handed than the singleborn was controversial for many years. Differences were attributed to inconsistent methods of classification between samples, perhaps because some early researchers were influenced by the belief that monozygotic (MZ) twins were likely to be mirror images and therefore one right- and one left-handed (McManus, 1980). Annett (1978) predicted that there should be a small increase in the frequency of left-handedness in twins, both dizygotic (DZ) and MZ, in comparison with the singleborn. The prediction followed from the discovery that the RS genetic model which explained handedness in families could also explain the distribution of twin pairs, provided the RS + gene was expressed a little less strongly in twins. The effect was not genetic, but environmental, due to limitation of gene expression during early growth. Very large samples drawn from the general population were needed to make the required comparisons. Davis and Annett (1994) found in a survey of over 30,000 people in the UK for hearing loss, aged 18 years to over 80 years, that the incidence of left-handed writing in the singleborn was 7.1%, and in twins 11.7%. This is about the level of difference required by the RS theory. Sicotte, Woods and Mazziotta (1999) confirmed by meta-analysis that the incidence of left-handedness is higher in twins than the singleborn, and to about the same extent in MZ and DZ pairs.

The handedness of twins is important for genetic theories of asymmetry because of the well-known distinction between MZ twins who are virtually genetically identical and DZ twins who share 50% of genes on average. Classic tests of genetic influence look for a much greater similarity between MZ than DZ twins.

However, both types of twin include more than 20% of pairs with one right and one left-hander (RL pairs). MZ pairs are more similar than DZ pairs but the effect is so small that it can be detected only in huge samples (Sicotte et al. 1999). These observations have led many to doubt there can be a genetic influence on handedness. However, the doubters ignore two important facts. First, the role of chance asymmetry is very large (the normal curves of Figure 1) and second, the genetic variability is very small. The variability is small not because the genetic influence is small, but rather because it is present in the majority of the population. Thus the proportion of genetic variability is small in comparison with the large chance variability. The conclusion that individuals differ for handedness mainly because of environmental influences (Orlebeke, Knol, Koopmans, Boomsma & Bleker, 1996; Tambs, Magnus & Berg, 1987) is correct because differences are mainly due to accidents of early development. But this does not imply that there is no genetic influence. A rather rough analogy would be to say that there are no genes for upright walking because MZ and DZ twins are all upright walkers. A difference does not show up if the relevant genes are universal in the population. Similarly, the RS + gene is present in over 80% of the population, including MZ and DZ twins (Annett, 2003).

Anatomical asymmetries of brain volumes were compared between RR and RL twin pairs by Geschwind, Miller, DeCarli and Carmelli (2002). If the RL pairs include more RS - - genotypes than RR pairs, then the role of chance should be greater in the former. Correlations between twins for cerebral asymmetries were smaller in RL pairs than RR pairs as predicted.

How early in development is the RS + gene likely to be expressed? Several influences in the perinatal and postnatal period have been suggested as causal in the

development of handedness, but even earlier asymmetries have been detected by ultrasound scanning of the foetus (Hepper, Shahidullah & White, 1991). Sucking of the right thumb was observed in 90% and the left thumb in 10% of foetuses from about 15 weeks of gestational age. Follow up of these children at 10-12 years of age showed a remarkable consistency of hand preference with foetal behaviour (Hepper, Wells & Lynch, 2005). Of 60 foetal right thumb suckers only one wrote with the left hand, and of 15 left thumb suckers 7 wrote with the left hand. These findings are consistent with the idea that there is a factor which induces a bias to the right, but in its' absence, there are random biases to either side. The chief implication for the RS theory is that the mechanism that induces RS operates at a very early stage of growth, before the cerebral cortex is developed. Although the evolutionary advantage which selected this asymmetry could depend on the benefits of left hemisphere specialisation, the mechanism itself precedes rather than follows from the growth of the cerebral hemispheres.

Are there developmental problems associated with the presence or absence of the RS + gene? From first formulating the theory in 1972 it was suggested that the factor that induces left hemisphere advantage in most people is one which assists speech acquisition. The idea that absence of the factor gives random laterality of both speech and handedness could solve some longstanding puzzles about the increased proportion of left- and mixed-handers in children with developmental problems of speech and reading (Orton, 1937). Some 18.5% of the population are expected to be RS - - genotypes and develop cerebral specialisations at random. Not all of the random combinations would be at risk for disorder, but some might be associated with difficulties in the acquisition of speech and in the representation of speech sounds.

These ideas have been explored in several studies of literacy in schoolchildren, and in those attending for remediation of reading and spelling problems. Poor phonology is the chief characteristic identified in most studies of dyslexics. Among children with poor phonology attending normal schools, but with good performance on other tests, some 23-31% were left-handed for writing (Smythe & Annett, 2006). However, not all dyslexics have poor phonology and some dyslexics are strongly right-handed.

Distinctions between poor readers with and without poor phonology reveal a dissociation for handedness such that the former are more likely to be left-handed and the latter more likely to be right-handed than children who are not poor readers (Annett, Eglinton & Smythe, 1996). A similar dissociation was found in undergraduates (Annett, 1999b).

The RS theory does not claim that the RS locus (when it is found) will be the only genetic influence on dyslexia and other specific language impairments. However, the RS locus is likely to interact with other threats to language and literacy. Inspection of the genotype distributions in Figure 1 shows that the majority of mixed- and left-handers carry the RS + gene and should not have the literacy problems associated with the RS - - genotype. When right- and left-handers are compared in general school samples, therefore, no differences are expected or found for language skills. However, children with specific difficulties of speech and literacy in school and clinic samples have an increased proportion of nonright-handers as predicted. When genotypes can be identified directly, effects for handedness should be strong.

Psychopathology

Raised incidences of nonright-handedness have been described for the learning disabled (Gordon, 1921; Pipe, 1990), epileptics (Bingley, 1958), criminals and

psychopaths (Bogaert, 2001), those with gender identity disorders (Zucker, Beaulieu, Bradby, Grimshaw & Wilcox, 2001), and homosexuality (Lalumière, Blanchard & Zucker, 2000; Lindsay, 1987). There have been three substantial meta-analyses of studies of schizophrenia, taking different criteria of hand preference, all of which find an excess of nonright preferences in schizophrenics (Dragovic & Hammond, 2005; Satz & Green, 1999; Sommer, Aleman, Ramsey, Bouma & Kahn, 2001). Raised incidences of nonright-handedness are also found in people with special talents including baseball, cricket and tennis professionals, artists, mathematicians, musicians and surgeons (Annett, 2002 for review). These lists show that handedness cannot be the cause of any of these conditions, healthy or pathological. It is wrong to treat handedness as a 'marker' for criminality, dyslexia, schizophrenia, or other condition. The vast majority of nonright-handers are healthy law-abiding people. The differences for groups listed above depend on very small statistical effects, in groups selected for the conditions of interest and detectable only in large samples. How could these small differences arise?

For those with special talents, the most probable explanation is a reduction of the effect of the RS + gene. If the effect of the gene is to weaken the left hand and right hemisphere, talents that depend on motor skill and enhanced right hemisphere function would be better performed by those of RS - - and RS + - genotype, in comparison with RS ++ genotypes. Annett (2002, chap. 12) found that the raised proportion of left-handers among tennis professionals, for example, is at the level expected if RS ++ genotypes were absent from this group (about 12-15% versus 8-10% in the general population). Similarly, artists, mathematicians and surgeons are likely to need well-functioning right as well as left hemispheres.

Studies of schizotypal thinking have often found higher scores among mixed-handers (Barnett & Corballis, 2002; Chapman & Chapman, 1987; Claridge, Clark, Davis & Mason, 1998) than consistent right-handers. Assessments of schizotypy usually depend on questionnaires about unusual types of thinking, such as having magical powers, or being watched. Annett and Moran (2006) investigated response to such questionnaires in over 700 undergraduates, assessed also for handedness. They found higher scores for schizotypy in groups defined as mixed-handers on several criteria. There was a particularly high score in one group, right-handed writers who perform other actions that Annett (1970) called 'primary' actions (throwing, racket, match, hammer, toothbrush) with the left hand. Among undergraduates unusual types of thinking may be associated with creativity. Mixed-handers in healthy samples should include a high proportion with heterozygote advantage for the RS locus.

How is nonright-handedness raised in those with the disadvantaged conditions listed above? The RS theory suggests that adverse influences on growth are likely to reduce the extent of RS, as discussed with respect to development. Handedness is not causal, but secondary to changes of cerebral growth due to pathology. Geschwind and Galaburda (1985a, 1985b, 1985c) reviewed a very large number of conditions associated with increased nonright-handedness, and speculated about many causes. There may be numerous specific developmental pathologies involved, but effects for handedness depend, on the RS hypothesis, on factors which interfere with normal growth and so reduce the expression of the RS + gene. In order to show that there is a genetic influence on these conditions, it would be necessary to show that there are also differences for handedness in the patients' relatives.

Orr, Cannon, Gilvarry, Jones & Murray (1999) found that *schizophrenics and their first degree relatives* had a raised proportion of mixed-handers, when the latter was defined as right- or left-handed writers who were inconsistent for other primary actions. Sharma et al. (1999) measured volumes of several cerebral regions and found asymmetries present in healthy controls, that were absent in schizophrenics and also absent in unaffected relatives who appeared to be obligate carriers of genetic liability. These findings suggest that reduced asymmetries in schizophrenics are due not only to developmental processes in the individual, but also involve some genetic influence. Might such an influence depend on the RS locus?

For some years Crow (1997) has suggested that schizophrenia is due to a loss of cerebral dominance, perhaps associated with the hypothesised RS+ gene. Annett (1997) proposed a possible mechanism, that the RS + gene mutates to a form which loses its directional coding. If the gene became unable to distinguish left and right, it could be said to be *agnosic* for directional asymmetry. ('Agnosic' means loss of recognition and is often wrongly corrected by spell-checkers to 'agnostic' which means lack of belief). The normal RS + gene is hypothesised to induce left hemisphere advantage by giving an instruction such as, 'Handicap one hemisphere, the right'. Suppose that a mutant form of the gene lost the last part of the instruction, it would now say 'Handicap one hemisphere' but leave unspecified which one. When paired with a normal RS - gene there would be one good hemisphere remaining and so no serious problem. When paired with an RS + gene with a normal instruction to impair the right hemisphere, there would be 50% of cases when the agnosic gene also attacked the right hemisphere (as in normal RS ++ genotypes). However, in 50% of cases, the agnosic gene would attack the left hemisphere, leaving both hemispheres

affected. Could this be a cause of schizophrenia? When the genetic risks were calculated in the light of RS model, as already worked out for handedness in families, with a prevalence of schizophrenia at about 1%, there was a striking match with the risks for relatives as estimated by Gottesman (1991). Further, the frequencies suggested that a double dose of the agnosic gene would occur in about 4 in 10,000 cases, about the rate estimated for strictly defined autism (Rutter, 1991). Many genes are being researched in the search for causes of schizophrenia and autism. It may well be that there are different routes to these disorders. However, an important advantage of the agnosic gene theory is that it allows the illness to depend on a stochastic process. One of the best established statistics for schizophrenia is that the risk to the co-twin of an MZ proband is about 50%. This is consistent with an agnosic gene that affects either hemisphere at random.

Conclusion

The RS theory is very simple in that it suggests there is only one specific influence on brain asymmetry, one which induces the typical pattern of cerebral specialisations and incidentally raises the probability of right-handedness. The theory is complex in that the implications of this idea have to be explored in relation to many topics for which laterality might be a relevant variable, and when outcomes depend on probabilities, not discrete categories. This process of exploration is by no means complete, and the theory can be expected to develop through further investigations.

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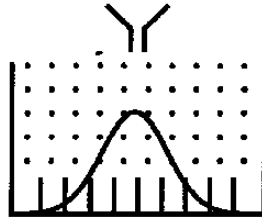
Handedness in boys with gender identity disorder. *Journal of Child Psychology and Psychiatry*, 42, 767-776.

Figure Caption

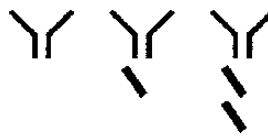
Figure 1. A schematic representation of the main elements of the right shift theory: see text for explanation (from Annett, 2000).

RIGHT SHIFT THEORY OF HAND AND BRAIN

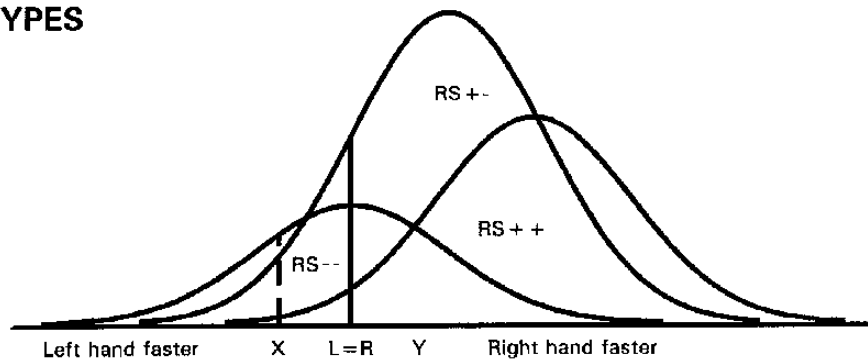
1. CHANCE



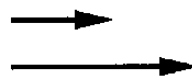
2. RS + GENE



3. GENOTYPES



4. SHIFT



5. THRESHOLDS

