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Is handedness related to health status?

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ABSTRACT

Handedness is the most important behavioural asymmetry due to its intimate association with the specialisation of the brain for language. It exists in 3 forms, namely right, left and mixed. Left-handers constitute the biggest minority group in the world and in many aspects they are in a disadvantaged position compared to right-handers. Numerous studies demonstrated association between left-handedness and different health problems ranging from learning disorders to breast cancer and decreased longevity. This paper reviews the relevant literature on the genesis of handedness and connection between handedness and health. Deviations from the "normal" pattern of braininess observed in some left-handers might contribute to developmental, cognitive and some mental disorders. However increased incidence of some of pathological conditions among sinistrals could hardly be explained by the "abnormal" pattern of braininess or by the action of a gene or genes responsible for handedness determination. Review of literature suggests that many of health problems of left-handers develop due to environmental, developmental and other mechanisms related to genesis of handedness.

Introduction

Enantiomorphic systems usually have two types of laterality, right and left. Sidedness is one of the behavioural manifestations of enantiomorphy. It includes handedness, eyedness, footedness and earedness among others. However handedness is the most important asymmetry due to its intimate association with the brain specialization for language.

Distribution of handedness in a population posses features of directional asymmetry in which non-recemic mixture of two types of laterality is found.[1] In human populations, there is a consistent tendency for the right hand to be the preferred hand as approximately 10% of people in most societies are left-handed.[1-4] This fact suggests that the shift to the right depends on systemic bias to the right hand rather than on accidental preference of the left hand.[1,2]

For centuries, right hand preference has been a behavioural norm and left-handers were the largest minority group in the world and were stigmatized culturally, socially and even linguistically. Therefore the important question related to the origin of handedness is what are the advantages of right-handedness? Several authors suggested that right-handedness evolved from the fact that it is more convenient to use right hand for such activities as carrying and comforting of a baby or for carrying and using weapons in early warfare.[5,6] The greater mortality of the left-handers in battles, then, is proposed as the mechanism driving the higher prevalence of right-handedness today. Development of hand preference was also necessary to increase speed and automaticity of manual activities for survival and stimulated lateralization of functions in the brain.[5] Therefore handedness and language are lateralized to the same hemisphere because they both require similar fine motor control. With speech development, left hemisphere received some advantages over the right one and became dominant in language based higher brain functions.

Association between handedness and braininess

The relationship between handedness and braininess is an issue that is at the center of many associated problems including biological consequences of handedness. Precise hand movements and language are two most highly skilled activities of the human being. Therefore it is not surprising that laterality for speech and handedness depend on each other. In majority of right-handed people language is lateralized to the left side of the brain, which is dominant in language-related higher brain functions.[7] The same hemisphere controls right hand movements. However up to 7.5% of normal right-handers have atypical language lateralization in the brain.[7,8] In 78% of left handed and ambidextrous people right side of the brain is dominant in language-based functions.[8] In the rest of non-right-handers language areas are located bilaterally or in the left hemisphere. The relationship between hand preference and cerebral lateralization of functions in non-right-handers is hampered by the heterogeneity of this group. Some left-handers prefer left hand for all behavioural activities. However many of non-right-handers have inconsistent hand use with the left hand preferred for some unimanual activities and the right hand for others. It should also be kept in mind that the cerebral cortex has considerable plasticity and it is too simplistic to say that the function is lateralized at one side only, as both sides of the brain work together in a highly coordinated and integrated manner.

Genesis of handedness

An important question on the origin of handedness is the nature of systematic bias that favors right hand preference. There is strong evidence of genetic predisposition to left- or right-handedness.[9] Developmental, intrauterine and other factors, which act prenatally might also play a role in the genesis of handedness so that neonates are lateralized (structurally, if not functionally) at birth.[6,10] Postnatal factors such as socio-cultural environment and learning play an important role in modification of handedness expression. For example, low prevalence of left-handedness in African and Asian populations could be attributed to the strong socio-cultural pressure against use of the right hand for unilateral activities rather than to the lower incidence of left-handedness itself.[11,12,13]

Many studies were devoted to the genetic origin of handedness. According to Annet, dextrality depends on a single Right Shift gene (RS+), which also facilitates the left hemisphere special-

ization for speech but at the expense of some right hemispheric functions.[2,3,14] RS- genotype of left-handers has random asymmetries for the brain and the hand. McManus introduced three-allele model of handedness.[1,15] However Right Shift theory better predicts distribution of handedness in families than McManus genetic theory. Many studies questioned simple genetic models of handedness as monozygotic twins appear to be substantially discordant.[4,9] Therefore a polygenetic explanation of handedness genesis might be more appropriate.[4] It takes into consideration more than one pair of alleles and cytoplasmic inheritance as well as developmental and environmental mechanisms which are driven by genetic factors.

Biological consequences of "abnormal" dominance pattern in left-handers

Many researches have emphasized the biological consequences of deviations from the "normal" dominance pattern (i.e. right-handedness with left-hemispheric linguistic dominance and right-hemispheric visuo-spatial dominance) observed in left-handers.[3,16-19] It was suggested that these deviations might explain increased prevalence of developmental, cognitive and some mental disorders among lefties. At the same time, detailed analysis of comprehensive list of groups of people with elevated prevalence of left-handedness[16] suggests that increased incidence of many of pathological conditions and health problems such as allergies, immune disorders, myasthenia gravis, ulcerative colitis, breast cancer, low birth weight, perinatal birth stress and many others observed in left-handers, could hardly be explained by the "abnormal" pattern of braininess or by the effects of genetic factors linked with genesis of handedness. To the best of our knowledge, there is no published evidence that a gene or genes, which are responsible for handedness determination and development, play a role in predisposing left-handers to specific pathological conditions. Two possible explanations could be employed to explain association between left-handedness and these health problems. Firstly, some of the studies on association between handedness and diseases were not replicated successfully. Therefore some of the correlations might be spurious. Secondly, it might be reasonable to suggest that developmental, endocrinological, environmental (intrauterine) and other factors which interfere with handedness determination could also affect health of the left-handed people. In this case, association between left-handedness and some diseases does not result from "abnormal" pattern of braininess and left-handedness itself but rather from effects of developmental, endocrinological and environmental factors which might have genetic origin. In order to test this hypothesis we review a literature on handedness origin and possible mechanisms of association between handedness and health.

"Pathological" left-handedness and health

Some authors suggested a pathological origin of left-handedness in children who have been genetically predisposed to be right-handed but switched to the left hand. "Birth stress or brain damage" theory states that the left hemisphere is more sensitive to intrauterine and neonatal pathological conditions such as hypoxia and birth stress and more vulnerable to the damage during birth process than the right hemisphere.[20] Damage to the left hemisphere might result in switch from the left to the right side in cerebral dominance. Therefore some (if not all) left-handedness is caused by damage of the left hemisphere during intranatal and neonatal periods. There is considerable evidence to support the theory. Birth complications are far more common among left-handers and babies with low Apgar scores have higher prevalence of left-handedness.[21,22] In addition, birth stress is associated with a number of disorders that are also related to left-handedness, including autism, epilepsy, cerebral palsy, Down's syndrome, mental retardation, strabismus and schizophrenia.[23] Therefore it is reasonable to suggest that damage to the left hemisphere, which causes pathological handedness in association with prematurity, low birth weight and birth stress facilitate manifestation of different diseases in left-handers.

Role of endocrinological factors in genesis of left-handedness and connection between handedness and health

The Geschwind-Galaburda testosterone theory (G-G) links the origin of left-handedness and increased level of effective testosterone due to genetic factors, increased sensitivity to testosterone, the presence of male co-twin, or an anomalous endocrine environment during pregnancy.[17-19] Increased testosterone level during intranatal development has numerous effects because of wide distribution of testosterone receptors in the brain and other organs. Elevations in testosterone level cause excessive delays in formation of the speech control centers of the left hemisphere, which lead to cessation in the normal lateralization of speech. The left-handed person could keep left-brain lateralization for speech, but learning disorders will result. Alternatively, the left-handed person might switch to the right-brain speech lateralization or have bilateral representation of language. These findings have medical implications.[24] Stroke in left-handers with bilateral representation of language is more likely to affect language function than in right-handers. At the same time, left-handed patients are more likely to recover affected language function, because they have some language areas on the unaffected side.

Elevated level of testosterone also explains association between left-handedness and immune disorders. Testosterone causes thymus suppression.[25] The thymus is an important link in proper immune development. A faulty thymus will lead to defects in the immune system, which is crucial for the body's defense against foreign substances. Lymphocytes recognize foreign substances and attack them. Many lymphocytes reside in the thymus. If the development of the thymus were hindered, the lymphocytes would also be hindered. Perhaps, they would be unable to recognize foreign matter. G-G theory suggests that the development of the immune system is altered in left-handedness causing immunological misbalance which leads to immune disorders and autoimmune conditions.[26]

Left-handedness and increased risk of traumas

Many studies have indicated that left-handedness is associated with increased risk of different types of injuries.[27-29] Lefties are six times likelier to die in an accident, and four times likelier to die while driving than righ-handers.[30] Several mechanisms might be responsible for increased prevalence of injuries among sinistrals.[27] Firstly, majority of unimanual activities is biased in favor of right-handers. Therefore left-handers have to use tools, devices and consumer items designed for right-handed usage. Many of left-handers tend to use both sides of the body for different behavioural activities. Therefore both sides of the body are exposed to traumas. Secondly, left-handers are more likely to be involved in potentially dangerous activities where trauma can easily be sustained compare to right-handers. Thirdly, attacking lefties have an advantage because they are able to hit an opponent from the left side but defending sinistrals are in disadvantage position. Therefore in confrontational activities when they have to defend themselves, the rate of traumatisation increases.

Left-handedness and longevity

Left-handedness has been associated with decreased longevity because of "decreased survival fitness." [31,32] According to this view, elevated accident susceptibility, birth stress related neuropathy, developmental delays and irregularities, and deficiencies in the immune system are the markers for "decreased survival fitness" of sinistrals. However these findings are controversial and not universal. Fatal accidents alone cannot account for dramatic fall in the prevalence of left-handedness among old people. In addition, some diseases associated with left-handedness are relatively rare and there is no evidence that left-handedness is associated with increased risk of common diseases such as malignancy, cerebrovascular and cardiovascular diseases.[33]

In many studies the conclusion on connection between longevity and left-handedness is based on the fact that prevalence of left-handers decreases with age. For example, study conducted in Norway has showed the prevalence of left handedness of 15% among young adults but only 1.7% in subjects older than 80 years.[34] It is likely that older age groups contain fewer left-handers not because they die earlier, but because many in the older generation were forced to become right-handed due strong cultural censorship against left-handed people. Nowadays society is more liberal about left-handedness which allow people who are naturally left-handed to express their hand preference. Therefore the decline in cultural censorship against left-handedness can explain differences in the proportion of left-handers among children and young adults and elders.

In conclusion, the area of handedness is filled with grey sports. Numerous theories were offered to explain the origin of handedness and connection between handedness and health but precise answer is yet to be found. Left-handedness has been associated with different health problems ranging from learning disorders to breast cancer and decreased longevity. Review of the relevant literature suggests that many of health problems of left-handers develop due to environmental, developmental and other mechanisms related to the genesis of handedness rather than due to direct actions of a gene or genes responsible for handedness determination or "abnormal" pattern of braininess in some of sinistrals.

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ERRATUM

In the *Malawi Medical Journal* Volume 15 Number 3 Table of Contents page, we erroneously listed D.K. Lewis as the first author of the paper; Perinatal mortality audit at Tikure Anbessa Teaching Hospital, Addis Ababa, Ethiopia: 1995–96. The authors of the paper should have been only E. Tadesse and B. Worku