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Etiological Aspect of Left-Handedness in Adolescents

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SUMMARY

Introduction Lateralization of brain functions such as language and manual dominance (hand preferences and fine motor control) are most likely under genetic control. However, this does not preclude the effect of various environmental factors on functional brain lateralization. A strong association of non-right-handedness (left- and mixed-handedness) with various neurodevelopmental conditions (e.g. schizophrenia, autism, Rett syndrome) implies that in some cases, non-right-handedness may be acquired rather than inherited (i.e., pathologically determined).

Objective The aim of the study was: (a) re-investigation of several known risk factors for left-handedness (age of mother and/or father, twin pregnancies, and birth order), and (b) examination of hitherto un-investigated factors (type of birth, Apgar score, maternal smoking during pregnancy).

Methods Putative, causative environmental agents for this shift in manual distributions are explored in a sample of 1031 high school students (404 males and 627 females) from Belgrade. Both pre-existing (age of parents, twin pregnancy, and birth order) and new (Apgar score, maternal smoking, type of birth) putative agents are examined.

Results We found that maternal smoking and low Apgar score (2-6) can significantly increase risk for left-handedness (p=0.046 and p=0.042, respectively). The remaining factors showed no significant association with left-handedness in adolescents.

Conclusion Our study clearly demonstrates that left-handedness may be related to maternal smoking during pregnancy and a low Apgar score on birth.

Keywords: left-handedness; adolescents; risk factors; Apgar score; maternal smoking during pregnancy

INTRODUCTION

There are several profound and consistent neuropsychological, anatomical, chemical and physiological intra-hemispheric differences within the brain. Despite voluminous evidence that the brain is asymmetrical across various domains (a captivating product of evolution in itself), popular imagination seems more easily entertained by visible behavioral asymmetry such as hand dominance. Hand dominance (both as hand skill and/or hand preference) is systematically related to brain structure and organization, but not in a straightforward way. There are many more different asymmetries in humans in addition to hand dominance, (e.g., footednees, ear dominance, or eye dominance), but these have been studied less vigorously than handedness [1]. One possible explanation for this is the stigma that was associated with left-handedness until recently. Right-handedness was the norm, a desirable trait to which unlucky left-handed children had to conform. Interestingly, some researchers still contribute to the "bad reputation" of left-handedness by calling it alinormal (term alinormal was introduced in the laterality literature by Coren in 1992 in order to attenuate his radical view, in which left-handedness is conceptualized as an abnormal biological trait.) [2].

There is no consensus about definition or prevalence of left-handedness in the general population, nor upon the etiology of handedness. Prevalences of left-handedness differ across various geographical and cultural regions, possibly because of different methodologies used to collect data, and range between 6 to 14 percent [3]. In Serbia, prevalence estimates of handedness (according to available studies) range from five to ten percent, depending on the socioeconomic development of a particular region, and on the local practice of forcing hand dominance [4]. One recent study [5] in a large sample of primary school children in Belgrade (N=2546), reports a prevalence of left-handedness as 7.6%. A study of Belgrade high school students (N=1189), found a slightly lower prevalence of 6.8%. This sample had significantly less left-handed female (4.8%) than male students (8.9%) [6].

First, there is no agreement as to what is the actual phenotype under investigation. In other words, researchers disagree on a few simple questions such as what precisely is hand dominance and how it is measured. Although answers may appear simple, the definition of

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hand dominance is still unclear. For example, it is as yet unresolved whether hand dominance is a continuously distributed trait [7], or a simple categorical phenomenon [8].

It is widely accepted that left-handedness in itself is not the result of pathological neurodevelopment, thus left-handedness cannot be conceptualized as a pathologic sign. All leading researchers in the field agree on this [8]. This consensus however, does not exclude a possibility that left-handedness may sometimes (in a minority of cases) have pathologic origins. Studies in various clinical populations with increased prevalence of left-handedness suggest a pathological etiology, e.g. dyslexia [9], autism [10], schizophrenia [11], epilepsy [12], and (especially) in patients with Rett syndrome [13]. In these populations the term pathological left-handedness syndrome (PLH syndrome) is used to create distance from inherited or 'natural' left-handedness, with the term introduced by Paul Satz et al. [14]. By definition pathological left-handers are those who have switched hand dominance due to early brain injury. The excess of left-handedness (or the lack of clear hand dominance, i.e., mixed-handedness) in the above mentioned clinical populations is commonly attributed to abnormal neurodevelopment.

In the laterality literature several risk factors are investigated. These factors are known to influence the probability of atypical lateralization of brain structures and functions and thus, indirectly, increase probability of pathologic left-handedness. One of the first factors investigated was birth stress [15]. This risk factor, defined by Bakan [16] as being first-born or fourth-born and later, is considered controversial and has received little support [17]. More rigorous attention was given to the Geschwind-Galaburda model [3] which involved hormonal changes during intrauterine development. At the root of this model lays the sex hormone testosterone, an excess of which is postulated to delay development of the left cerebral hemisphere. Additional and various potential risk factors such as; maternal age [18], twin pregnancy [19], anxiety of mother prior to pregnancy [20], psychological stress during pregnancy [21], very low birth weight [22] and even ultrasound tests during pregnancy [23] have supplemented the Geschwind-Galaburda model.

Etiology of left-handedness is still not fully understood and for the most of risk factors there is limited scientific evidence [7].

OBJECTIVE

The rationale for this study was to further clarify the role of the most relevant epidemiological risk factors for left-handedness. Also, we wanted to test a hypothesis of the potential impact of other, previously not investigated risk factors. Our study on a Serbian adolescent population was aimed at: (a) re-investigation of several known risk factors for left-handedness (age of mother and/or father, twin pregnancies, and birth order), and (b) examination of hitherto un-investigated factors (type of birth, Apgar score, maternal smoking during pregnancy).

METHODS

The study sample comprised 1031 participants from five high schools from New Belgrade Municipality, Serbia, with 404 male and 627 female students (mean age 16.2 years, SD=1.2). Data were collected in collaboration with school psychologists. One high school invited to participate in this project refused. Out of 4100 questionnaires distributed, 1031 were returned (response rate of 25.14%) Table 1 presents distribution by year of students from five high schools. Data collected were anonymous and collected during class, with all students receiving identical instructions about collecting the information about pregnancy, delivery and Apgar score from their mothers before.

The study questionnaire comprised 21 items, divided into two parts, namely: (1) demographics and general characteristics (school, grade, date of birth, hand preference, maternal age on delivery, paternal age on child's birth) of students and parents, and (2) medical information such as type of birth (natural, caesarean procedure planned and unplanned, vacuum and use of forceps), twin pregnancy (yes or no), birth order, maternal smoking during pregnancy and Apgar score. Due to small frequencies, all non-natural births were combined in a single category. Apgar score is a standardized, simple and reliable measure to assess the health of a baby using a three-point scale to assess five parameters (skin color, pulse rate, reflex irritability, muscle tone, breathing). Total Apgar score ranges from 1 to 10, whereby 10 means desirable, almost ideal health of a newborn. Newborn babies with Apgar scores less than 7 are considered to be at health risk, and usually require specialized medical attention. Prior to statistical analyses, each student's Apgar score was dichotomised as being normal (7-10) or risk (2-6). Birth order was also dichotomised into: first born and fourth born and later (high risk) versus 2nd and 3rd born (low risk). All analyses are conducted using SPSS version 17.

RESULTS

Prevalence of left-handedness in our sample was 11.2% (n=115), with disproportionally more males (13.6%) than females (9.4%) being left-handed, χ^2=4.91, df=1, p=0.027.

To assess potential effect of age of both parents on left-handedness, we used binary logistic regression. Overall, we found that age of parent was significantly associated

Table 1. Distribution of students by corresponding high schools (New Belgrade)

School	Class				Total
	I	II	III	IV	
IX Gymnasium	19	55	9	39	122
X Gymnasium	129	74	884	44	331
Touristic High School	108	67	90	58	323
Technical High School	41	42	30	31	144
Polytechnic High School	33	40	29	9	111
Total	330	278	242	181	1031

Table 2. Prevalences and odds ratios (OR) for selected risk factors (binary logistic regression)

Risk factor		Left-handed (%)	Right-handed (%)	OR	95%CI	p
Twin pregnancy	Yes	2 (7.1)	26 (92.9)	0.61	(0.14-2.59)	0.499
	No	113 (11.3)	890 (88.7)			
Order of birth	1st, 4th and later	59 (10.1)	524 (89.9)	0.79	(0.53-1.16)	0.225
	2nd and 3rd	56 (12.5)	391 (87.5)			
Delivery	Unnatural	12 (8.5)	130 (91.5)	0.70	(0.38-1.32)	0.273
	Natural	103 (11.6)	786 (88.4)			
Apgar score	Low (2–6)	4 (16.7)	20 (83.3)	1.67	(0.56-4.99)	0.357
	Normal (7–10)	99 (10.7)	828 (89.3)			
Smoking during pregnancy	Yes	36 (15.1)	203 (84.9)	1.50	(1.01-2.24)	0.046
	No	79 (10.0)	712 (90.0)			

CI – confidence interval

with left-handedness in children, χ^2=6.08, df=2, p=0.048. Accordingly, the proportion of explained variance in the dependent variable was low, R^2=0.012 with odds ratios for left-handedness marginally increased for paternal age, OR=1.034 (95%CI 0.99-1.07), p=0.059, but not maternal age, OR=1.022 (95%CI 0.98-1.06), p=0.277. An independent-samples t-test comparing maternal age in left- and right-handed students found no significant difference, t(1029)=1.09, p=0.277. A comparison of paternal age in left- and right-handed students showed that the mean age of fathers of left-handed students was higher (M=32.2, SD=6.3) than of fathers of right-handed students (M=30.9, SD=5.3). That difference nominally was not statistically significant, t(1029)=1.89, p=0.059. For fathers, we also found a significant difference in age distribution, F(1,1030)=1.39, p=0.013. Accordingly, the effect size (Cohen's d statistic) of age difference for fathers was small (d=0.223).

The remaining risk factors were examined using the Mantel-Haenszel test to estimate common odds ratios. The results are presented in Table 2.

The sole significant association was that of left-handedness of children and a mother's smoking during pregnancy. Since an Apgar score is effectively an ordinal scale, with the data not normally distributed (Kolmogorov-Smirnov Z test= 8.81; p<0.0001) we used the Mann-Whitney test (non-parametric analogue to t-test) to investigate whether left- and right-handed students differ on Apgar score. The results showed that left-handed students had significantly lower average rank (429) than right-handed students (482), and thus had significantly lower Apgar scores, Z-statistic=-2.04, p=0.042.

DISCUSSION

This study expands the existing list of risk factors for the occurrence of left-handedness. In a large cohort of high school students we found that the low Apgar score (<7) and smoking of mother during pregnancy increased the probability for left-handedness. The remaining risk factors that we investigated (parental age, unfavorable birth order, unnatural birth, and twin pregnancy) showed no association with left-handedness.

Paternal age as a putative risk factor for left-handedness only approached statistical significance and the size of this effect was rather small. Expectedly, left-handedness was significantly more prevalent in male than in female students. Gender difference in manual lateralization is highly replicated finding, with males having more left-handers than females [7]. Overall, we believe that our study lends some support for PLH syndrome.

There were several investigated risk factors that showed no association with left-handedness in students. Maternal age has frequently been investigated as a putative risk factor for left-handedness, especially age of mother during pregnancy [24]. In brief, there is wide agreement that parental age does not have a direct influence on hand dominance in children. Recently, in a similar and large sample of high school students [24] no statistically significant association between parental age and left-handedness was observed. Age of father has rarely been investigated. We are prone to believe that weak (in terms of statistical power) and yet non-significant association in our study points to a statistical artefact rather than a true causal relationship. Neither twin pregnancy, nor birth order, were associated with increased prevalence of left-handedness as risk factors and this is in accordance with the findings of Medland et al. [25].

Our results are consistent with numerous studies failing to support the birth-stress model [25]. Type of delivery is a potential risk factor for left-handedness which has been rarely investigated. It has been argued that boys born by breech delivery are more likely to be left-handed [26]. Our study however, has failed to identify a link between the type of delivery and left-handedness, possibly because of combining various small numbers of unnatural births into a single, non-specific and heterogeneous category.

Associations between the Apgar score, both as a general indicator of newborns' physical health, and as an indicator of left-handedness is potentially very interesting. Firstly, it is known already from human [27] and animal [28] studies that stress during pregnancy could have long term harmful effects on a progeny's neurological development. Stress during pregnancy can be caused by various factors such as preterm birth, low birth weight, twin birth, respiratory distress syndrome or rhesus incompatibility. Apgar score

appears as a global substitute for a range of isolated factors, amongst which oxygen deprivation (asphyxia) appears to have the most harmful effect. One of the largest epidemiological studies [29] on a sample of almost 7,000 children reported almost doubled prevalence of left-handedness in children who required resuscitation as babies. In this study all common confounders such as various demographic factors as well as familial left-handedness were controlled. Several other influential studies [22], have unequivocally confirmed a link between atypical lateralization and extremely low birth weight. Similarly, a recent epidemiological study [30] reported that left and mixed-handed children perform significantly worse in nearly all measures of psycho-physiological development than right-handed children. All these studies suggest that an Apgar score can effectively serve as a composite measure of birth stress in future research, as it is available for almost every child and is easily retrievable from medical databases.

Maternal smoking during pregnancy and left-handedness has rarely been investigated, despite the fact that smoking has a deleterious effect on brain development. A recent study [31] has shown that prenatal exposure to smoking affects brain neurophysiology. An earlier study [32] showed that maternal smoking is significantly associated with a shift to the left in the handedness distribution. In our study we also found that smoking of mother during pregnancy is linked to left-handedness. It should be acknowledged however, that there is at least one (to our knowledge) study reporting negative results [33].

The model of PLH introduces important distinctions between natural and pathological left-handedness, suggesting that pathological left-handedness is acquired rather than inherited due to brain injury (e.g. prenatal hypoxia), possibly to the left cerebral hemisphere during early development. As such, the PLH model is able to explain why in certain populations there is an increased prevalence of left-handed individuals. This model however, precludes radical views such as Coren's [2] construct of alinormality, which was widely rejected (including in the present authors' recent study, i.e. Milenković, et al. [5]. It is also consistent with the leading theory in the field, e.g. Annett's Right Shift Theory [7], which sees left-handedness as a more variable normal (except pathological cases) variant of the lateralization of hand preferences. This specific variant is a heterogeneous phenotype, associated occasionally with unfavorable medical conditions (autism, Rett syndrome, schizophrenia, etc.), but it is also associated with favorable behaviors such as art (Leonardo da Vinci, Michelangelo, Picasso), music (Paul McCartney), science (Albert Einstein), and sport (Maradona, Rafael Nadal), to name but a few human activities in which left-handers are overrepresented. This biological advantage associated with left-handedness, explains perhaps (despite associated costs) why left-handedness is not selected out through evolution.

CONCLUSION

Overall, our study lends some support for the concept of pathological left-handedness. Our study clearly demonstrates that left-handedness may be related to maternal smoking during pregnancy and a low Apgar score on birth. The public health message that emerges from these findings is clear especially with regard to maternal smoking during pregnancy. These findings are supported by theories based on factors affecting intrauterine development and birth stress in the etiology of left-handedness.

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Етиолошки аспект леворукости код адолесцената

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КРАТАК САДРЖАЈ

Увод Латерализација мождaних функција као што су језик и доминантност руке (предност једне руке и фина моторна контрола) углавном је генетски контролисана. Међутим, ово не спречава утицаје различитих спољашњих фактора на мождану латерализацију. Снажна повезаност „недесноруκости" (леворукости и мешане доминације) и различитих неуроразвојних стања (на пример, схизофренија, аутизам, Ретов синдром) подразумева да у неким случајевима недесноруκост може бити пре стечена него наслеђена (патолошки одређена).

Циљ рада Циљ рада је било поновно испитивање неколико познатих фактора ризика за леворукост (старост мајке и/или оца, близаначка трудноћа и редослед рођења) и истраживање досад неиспитаних фактора (врста порођаја, Апгар скор, пушење мајке током трудноће).

Методе рада Наводни узрочни агенси из спољашње средине за ову измену у мануелној дистрибуцији истражени су на узорку од 1.031 ученика средњих школа (404 мушког и 627 женског пола) из Београда. Испитани су набројани познати и нови фактори ризика за леворукост.

Резултати Утврђено је да ако је мајка пушила цигарете током трудноће, то може значајно повећати ризик за леворукост (p=0,046), а ризик такође може повећати Апгар скор између 2 и 6 (p=0,042). Остали посматрани фактори нису указали на значајну повезаност с леворукошћу код адолесцената.

Закључак Наше истраживање је јасно показало да леворукост детета може бити повезана с пушењем у трудноћи и са ниским Апгар скором на рођењу.

Кључне речи: леворукост; адолесценти; фактори ризика; Апгар скор; пушење; трудноћа

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