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Origins of Handedness: A nationwide study of 30161 adults

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Abstract

The origins of human handedness remain unknown. Genetic theories of handedness have received much attention, but some twin studies suggest modest, perhaps negligible genetic effects on handedness. A related question concerning handedness is whether twins have higher rates of left-handedness than do singletons. We studied handedness, with information on forced right-handedness, in a sample of 30,161 subjects aged 18–69 from a questionnaire survey of the older Finnish Twin Cohort. Left-handedness was found to be more common in twins (8.1%) and triplets (7.1%) than in singletons (5.8%), whereas ambidextrousness was more common in triplets (6.4%) than in twins (3.4%) and singletons (3.5%). As in many other studies, males were more likely to be left-handed. Ambidextrous subjects were more likely to become right-handed writers even if not forced to use their right hand. We fit maximum likelihood models to our twin data to estimate the contribution of additive genetic, common environment and unique environmental effects to hand preference. Results, depending on the model, indicate that unique environmental effects account for most observed variance in handedness, both in childhood (92–100%) and adulthood (74–86%). When forced right-handedness was taken into account, estimates of familial effects increased. Concordance for left-handedness in twins is rare, and accordingly, very large samples are needed to detect the familial effects. Our results show that forced-handedness can have an effect on estimates of genetic effects.

Keywords

ambidextrousness; forced handedness; genetic effects; left-handedness; twins

1. Introduction

Most humans are right-handed while a minority are left-handed or ambidextrous, although the incidence of left-handedness can vary in different cultures (Perelle & Ehrman, 2005). Left-handedness is more common in males than in females. Studies have indicated that the rate of left-handedness is approximately 13% in males and 11% in females (Gilbert & Wysocki, 1992; Peters, Reimers, & Manning, 2006). Handedness has been studied for years and several

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theories of the origins of left-handedness have been proposed, yet the determinants of human handedness are not clearly known.

It is suggested that left-handedness can be attributed to pregnancy and birth risk factors. A theory of pathological left-handedness has gained support, for example, from observations that left-handedness is over represented in schizophrenic patients (Dragovic & Hammond, 2005) or after childhood meningitis (Ramadhani et al., 2006). Also, one study indicated that left-handedness, at five years age, was almost two times more likely in infants who had required resuscitation after delivery (Williams, Buss, & Eskenazi, 1992). But another study in contrast indicated that of 25 potential pregnancy or birth stressors, only maternal age had a weak association with left-handedness (Bailey & McKeever, 2004). One factor that may relate to pregnancy risk events is seasonal variation in viral infections. Two studies with small samples (Martin & Jones, 1999; Nicholls, 1998) have yielded contradictory results, while a study of >15 000 subjects found no evidence of a relationship between handedness and season of birth (Cosenza & Mingoti, 1995).

While some studies have found increased left-handedness in twins and triplets compared to singletons (for a meta analysis see Sicotte, Woods, & Mazziotta, 1999; Williams et al., 1992), a more recent study of large numbers of twins and their siblings found no difference in left-handedness between twins and singleton sibs (Medland et al., 2003). Some speculate that the higher rate of left-handedness in twins and triplets results from their more stressful pregnancy and traumatic delivery (Sicotte et al., 1999). Yet, even if stressors related to pregnancy or birth trauma account for some left-handedness, not all left-handedness is of pathological origin. Thus, the origins of left-handedness in healthy humans remain unclear.

Many studies have observed handedness postnatally, but ultrasound studies suggest that the formation of handedness takes place prenatally. Right hand preference, in the form of thumb sucking, occurs already in fetuses at 10 weeks gestational age (Hepper, McCartney, & Shannon, 1998). Prenatal thumb sucking, observed by ultrasound, has been related to head position preference in newborns (Hepper, Shahidullah, & White, 1991) and even to handedness at age 10–12 (Hepper, Wells, & Lynch, 2005). These ultrasound studies strongly support the early formation of human handedness.

Two common genetic theories of handedness propose that a single gene is responsible for handedness (Annett, 1998; McManus, 1985). The single gene with two alleles [rs+/rs- in Annett's right shift theory and C (change)/D (dextral) in McManus' symmetric bimodal model] is not directly related to left- versus right-handedness: instead, it determines whether there is liability to right-handedness or no liability to either side. RS+ or D homozygotes have a strong liability to right handedness, while rs- or C homozygotes lack a liability to either side and accordingly have greater probability to be left-handed. Although there is familial aggregation of left-handedness, these genetic theories are inadequate to explain the formation of handedness. A study of over 12 000 subjects reported that 76% of right-handed and 61% of left-handed subjects had no left-handed first degree relatives (Perelle & Ehrman, 1994). Based on data on over 72 000 offspring, the prevalence of left-handed offspring was about 26% given two left-handed parents, about 20% given one right-handed and one left-handed parent and about 10% given two right-handed parents (McManus & Bryden, 1992), results that cannot be explained by a Mendelian model. In fact, there is evidence that many genes might influence handedness (Francks et al., 2002). Although genetic models of handedness have been given much attention, many twin studies of handedness have yielded inconsistent results. Some twin studies have indicated genetic effects (Geschwind, Miller, DeCarli, & Carmelli, 2002), but many others have found very small or no genetic effects on handedness (Ooki, 2005; Ross, Jaffe, Collins, Page, & Robinette, 1999; Su, Kuo, Lin, & Chen, 2005). A recent meta-analysis from 35 samples of twins indicated that additive genetic effects account for 25% (95%

Confidence Intervals 16–30%), and unique environmental effects account for the remainder of the variance in handedness (Medland, Duffy, Wright, Geffen, & Martin, 2006). Similarly, a large study of twins and their family members from Australia and the Netherlands estimates that 25% of the variance in handedness is attributable to additive genetic effects (Medland et al., 2008). Previous twin studies have some limitations. The studies that involve older aged subjects have not taken into account the fact that some of the right-handed individuals are naturally left-handed but were encouraged, or even forced, to use their right hand. Additionally, many studies have not carefully characterized ambidextrous persons, but instead have dichotomized all participants into right- versus left-handedness.

The purpose of the present study is to analyse several aspects of handedness in a large, informative data set consisting of singletons, twins and triplets. First, we study whether the prevalence of left-handedness and ambidextrousness differs in singletons, twins and triplets. Second, we estimate the relative proportions of genetic and environmental effects on handedness, with consideration of having been forced to change handedness.

2. Methods

2.1. Subjects

The studied sample was based on the older Finnish Twin Cohort Study, which includes all Finnish same-sex twin pairs born before 1958 with both twins alive at the compilation of the data set (Kaprio & Koskenvuo, 2002). Candidate twins were identified from the files of Population Register Centre of Finland. A questionnaire was mailed in 1975 to all subjects who satisfied the criteria for twin pair selection, namely pairs of persons born on the same day, born in the same local municipality and had the same surname at birth. Twinship was defined by questionnaire responses and confirmed when needed from local parish records. The zygosity diagnosis was based on an accurate questionnaire method validated using genetic markers (Sarna, Kaprio, Sistonen, & Koskenvuo, 1978). The response rate was 89%. We excluded subjects who were 70 years or older from these analyses, thus leaving 30161 subjects for the handedness analyses. There were singletons ($n=4068$), who were subjects who fulfilled the selection criteria but were not biological twins, same-sex twins ($n=25810$) and triplets ($n=283$). There were 7430 monozygotic twins (MZ), 16462 dizygotic twins (DZ) and 1918 twins whose zygosity was uncertain. For the genetic analyses there were 10830 total pairs with known zygosity.

Because we did not have longitudinal data on handedness in the older Finnish Twin Cohort Study, we used another Finnish twin sample, which has longitudinal handedness information, to study the validity and the stability of childhood handedness reports. FinnTwin12 is a population based twin study that consists of Finnish twins born in 1983–1987 (Kaprio, Pulkkinen, & Rose, 2002). We had data for 532 twins, where twins first reported their handedness at age 14 and later when they were 21–24 years old. At age 14, handedness was measured by questionnaire: subjects were asked to indicate whether they are right-handed, left-handed or ambidextrous. Further the writing hand, right/left, was asked, as well. At age 21–24, handedness was measured with the 10 item Edinburgh Handedness Inventory (EHI) (Oldfield, 1971), which yields a laterality quotient (LQ) that ranges from -100 (totally left-handed) to $+100$ (totally right-handed). LQ was calculated by subtracting the left hand score from right hand score then divided by 20 and that result was further multiplied by 100. The stability of writing handedness from age 14 to age 21–24 was studied by plotting receiver operating characteristic (ROC) curve after using logistic regression analysis.

The older twin cohort study was approved by the National Board of Health of Finland. As a questionnaire study, the study purpose was explained to the participants in the cover letter requesting their participation. Returning a questionnaire was considered to indicate consent.

Further feedback has been provided regularly after the questionnaire study and participants have been permitted to withdraw from the study at any point. The FinnTwin12 study protocol was approved by the ethical committee of the Helsinki and Uusimaa Hospital District, and by the IRB of Indiana University, Bloomington, In.

2.2. Handedness measures

Handedness was assessed with two questions: 1) as a child, were you right-handed, left-handed or used your both hands equally; 2) at the moment, are you writing with right-hand? No or yes. In addition, subjects were asked: “if you were left-handed as a child, were you forced to write with right hand? No or yes”. The birth order was asked from both of the twins: “Which one of you. You or your co-twin was born first? My co-twin, me, I don’t know”. For birth order variable, we used only those pairs (n=9083) who were congruent with respect to their birth order report. Due to missing data in handedness measures, the number of subjects in analyses of individuals varied from 29759 to 30152 subjects.

2.3. Data analysis

The differences in handedness by sex, twinship status, zygosity and birth order, were analyzed with chi-square statistics using STATA software (Stata, 2006). The clustered data were taken into account whenever twins or triplets were included in the analysis. Thus we used cluster corrected *F*-value instead of uncorrected chi-square value. Genetic univariate modelling was done with Mx software (Neale, Boker, Xie, & Maes, 2003). Univariate models were conducted based on contingency tables, and we used the maximum likelihood method to estimate the variance components for additive genetic (A), shared environmental (C) and unique environmental (E) effects. We also used sex-limitation modelling to test for differences in the male and female components of variance. The estimation of familial (A and C) effects is based on the assumption that in MZ twins the correlation of additive genetic effects is 1.0, and 0.5 in DZ twins, who share on average half of their segregating genes. The correlation between common environmental effects is 1.0 both in MZ and DZ twins (see Figure 1) representing exposures and experiences influencing both twins. The unique environmental effects refer to all environmental effects that are unique to each individual and thus are uncorrelated between co-twins. The E component also includes the measurement error. In genetic modelling, the phenotypic variance is decomposed to A, C and E components. First we performed the full ACE model and after that we dropped each component at a time and then tested whether the dropping of a parameter reduces the model fit. All models AE, CE and E were compared to full ACE model. The comparison of the models was based on the X^2 and Akaike’s Information Criterion (AIC) statistics. If the p-value of the model reached significance at 0.05 level the model could be dropped. In AIC the smaller number refers to better fit. Power calculations for detecting the additive genetic and common environmental effects were calculated by using the method described in Visscher (2004) and Visscher, Gordon and Neale (2008).

3. Results

3.1. Stability of handedness in the FinnTwin12 sample

Based on the ROC curve value of 0.944, writing handedness in childhood was a good predictor of the LQ in adulthood in FinnTwin12 sample. The distribution of LQ by childhood handedness showed that within right-handers, only one from 467 right-handed subjects scored LQ less than 0 and within 59 left-handers there were six subjects who scored higher than 0. There were only six ambidextrous subjects: three of them were ambidextrous also in adulthood whereas other three subjects were categorized right-handed by EHI (see Figure 2).

3.2. Right-handedness, left-handedness and ambidextrousness in the adult cohort

Most of the subjects (88.8%) were right-handed as a child, while 7.8% were left-handed and 3.4% were ambidextrous. The vast majority (94.1%) were current right-hand writers, and 5.9% were left-hand writers (Table 1). Of the left-handed subjects, 48.5 % had been forced to use their right hand, and 21.5 % of the ambidextrous persons had been forced to use their right hand while only 0.9 % of subjects who indicated themselves as right-handed in childhood reported that they had been forced to use their right hand. The stability of handedness from childhood into adulthood by forced handedness status for all subjects can be seen from Table 2 and for twins in Table 3.

3.3. Handedness and age

Childhood left-handedness decreased slightly (from 8.8% in 18–19 year olds to 6.9% in 60–69 year olds) in older age groups, whereas childhood ambidextrousness increased (from 2.8% in 18–19 year olds to 4.8% in 60–69 year olds) in older cohorts ($F(10,170000) = 6.26, p < .0001$). Also the number of left-handed writers in adulthood decreased (from 8.8% in 18–19 year olds to 3.0% in 60–69 year olds) with respect to older cohorts ($F(5,86617) = 40.54, p < .0001$). Within left-handers, the proportion of forced right-handedness increased (from 20.9% in 18–19 year olds to 60.3% in 60–69 year olds) in older cohorts ($F(5,11219) = 42.47, p < .0001$). The proportion of childhood left-handedness (from 7.2% in 18–19 year old to 2.9% in 60–69 year olds, ($F(10,170000) = 20.82, p < .0001$) and adult left-handed writers (from 7.7% in 18–19 year olds to 2.6% in 60–69 year olds, ($F(5,83779) = 32.45, p < .0001$) decreased in older age groups similarly when we included only those subjects who were not forced to use their right hand. The proportion of left-handedness, ambidextrousness and forced right-handedness for different age groups can be seen from Table 4. The differences in age groups were evident similarly when males and females were considered separately (data not shown).

3.4. Sex differences in handedness

There was a higher prevalence of left-handedness in males than in females both in childhood (8.7% vs. 6.8%) ($F(2,34660) = 18.41, p < .0001$) and in current adult handedness (6.7% vs. 5%) measures ($F(1,17332) = 37.31, p < .0001$). This sex difference was also evident when singletons (7.3% vs. 4.2%) ($F(2,6210) = 9.20, p < .001$) and twins (8.9% vs. 7.3%) ($F(2,28215) = 12.09, p < .0001$), were considered separately. A sex difference of similar magnitude in triplets (8.1% vs. 6.1%) did not reach statistical significance ($F(2,291) = 0.46, p = .63$). There was no sex difference in ambidextrousness (3.3% in males and 3.5% in females) ($F(1, 16921) = 0.21, p = .64$). Further, within left-handers, there was no sex difference in forced right-handedness within all subjects (46.7 % in males and 50.6% in females) ($F(1, 2244) = 3.36, p = .07$) or in singletons ($F(1, 230) = 0.24, p = .63$), twins ($F(1, 1995) = 2.83, p = .09$) or triplets ($F(1, 17) = 1.69, p = .21$) separately. The sex difference in left-handedness was evident also when age groups were considered separately (data not shown).

3.5. Comparison of handedness prevalence in singletons, twins and triplets

Measured by childhood handedness, twins (8.1%) and triplets (7.1%) were more likely to be left-handed than singletons (5.8%) and ambidextrousness was more common in triplets (6.4%) than in twins (3.4%) and singletons (3.5%) ($F(4,69142) = 8.14, p < .0001$). In the same way, measured by the current writing hand, twins (6.1%) and triplets (6.4%) were more often left-handed than singletons (4.5%) ($F(2,34533) = 7.15, p < .001$). Within left-handers, there were no differences in forced right-handedness between singletons, twins and triplets ($F(2,4486) = 0.44, p = .64$). The differences were similar when age groups were studied separately (data not shown).

3.6. Twin analyses

There were differences between first (5.3%) and second born twins (4.8%) in the prevalence of left-handedness and ambidextrousness (3.1% vs. 2.6%) ($F(2,18156) = 3.22, p < .05$), but when ambidextrousness was left out of the analysis, the difference in left-handedness was not significant ($F(1,9065) = 2.36, p = 0.12$). For current writing hand, there was no difference in handedness between first born (5.4%) and second born (5.0%) twins ($F(1,9082) = 2.18, p = 0.14$). Nor was there a difference ($F(1,871) = 2.28, p = 0.13$), in twins who were left-handed as children, in forced right-handedness between first and second born twins (27.4% vs. 31.8%). There were no differences in the prevalence of left-handedness between MZ and DZ twins in childhood handedness (7.9% vs. 8.0%) ($F(2,26104) = 1.13, p = 0.32$) or in current writing handedness (6.1% vs. 6.0%) ($F(1,13055) = 0.01, p = 0.93$). Similarly, ambidextrousness did not differ between MZ (3.0%) and DZ (3.4%) twins ($F(2,26104) = 1.13, p = 0.32$). Within left-handers, forced right-handedness was equally common in MZ (51%) and DZ twins (47%) ($F(1,1828) = 1.51, p = 0.22$).

3.6.1. Univariate genetic analyses for childhood handedness—Genetic modelling for childhood handedness was based on the contingency tables (Table 5). For right- versus left-handed subjects, the most parsimonious models were AE and E models. In the AE model, additive genetic effects accounted for 7% and unique environmental effects 93% of the variance in liability to left-handedness. In the CE model, common environmental effects explained 2% of the variance. When ambidextrous subjects were combined with the left-handed group, most of the variance was explained by unique environmental effects. In the AE model, additive genetic effects accounted only for 2% of the variance. In contrast, when ambidextrous persons were included in the right-handed group, additive genetic effects increased and the most parsimonious model was an AE model in which additive genetic effects explained 8% and unique environmental effects 92% of the variance. An alternative CE model, where common environmental effects explained 3% and unique environmental effects 97% of the variance, also fit the observed data. The full ACE model also fitted the data, but common environmental effects did not explain any of the variance (Table 7.). Because of the sex difference in the prevalence of left-handedness, sex limitation models were fit also, but there were no differences between male and female variance components.

3.6.2. Univariate analyses for current writing hand—For reports of current writing hand, both AE and CE models adequately fit the data (Table 7). When forced handedness was not taken into account in an AE model, additive genetic effects explained 21% and unique environmental effects 79% of the variance, and in the alternative CE model, common environmental effects explained 14% and unique environmental effects 86% of the variance. In a full ACE model, additive genetic effects explained 19% and common environmental effects 1% of the variance. In that ACE model, the power to detect additive genetic effects was 0.999 and 0.132 for detecting common environmental effects. When forced-handedness was controlled for by omitting all subjects who reported that they have been forced to use their right hand or reported hand change from left to right or vice versa even if they were not forced to use their right hand (see Table 3. for included groups and Table 6. for contingency tables) the estimates of familial effects increased. In AE model, additive genetic effects accounted for 26% and in CE model common environmental effects accounted for 18% of the variance (Table 7). In the full ACE model additive genetic effects explained 24% and common environmental effects 2% of the variance. In the ACE model, the power to detect additive genetic effects was 1.0 and 0.192 for detecting common environmental effects. Because of the sex difference in the prevalence of left-handedness, sex limitation models were fit also, but there were no differences between male and female variance components. Due to small number of concordant twin pairs for left-handedness, we were not able to perform separate genetic modelling for different age groups.

4. Discussion

Our results indicate that left-handedness was more common in twins and triplets compared to singletons, and ambidextrousness was more common in triplets compared to twins and singletons. In genetic modelling, the genetic effects increased when forced handedness was taken into account, but still only a quarter of the variance in liability to handedness was explained by additive genetic effects.

4.1. Prevalence of left-handedness and ambidextrousness

Left-handedness in our sample was somewhat less common than in other large scale studies (Medland et al., 2003; Ooki, 2005). The prevalence of left-handedness is typically considered to be about 10% (Perelle & Ehrman, 2005). In fact, the proportion of non right-handed subjects in our sample was 11.2% whereas only 5.8% were left-handed writers. Many of our subjects were born in the beginning of the 20th century when attitudes towards left-handedness may have differed from those of today. Even if we had a question concerning the forced handedness, many subjects might have been under pressure of using their right-hand, especially for writing, but have not reported it retrospectively. The forced-handedness within left-handers was much more common with older subjects in our study, and there was also a decrease in left-handedness, especially in adult writing hand, where the prevalence of left-handedness was almost three times higher in the youngest age group compared to the oldest age group. The fact that left-handedness was less prevalent also among those subjects who did not report forced right-handedness might indicate that there had been an atmosphere in favour of right-handedness. The other theory for reduced number of left-handers in older persons is the decreased survival fitness (Coren & Halpern, 1991), but this hypothesis has not been supported by study that found no difference in survival between right-handed and non-right-handed twins (Basso et al., 2002).

Many studies have divided subjects into right and non-right-handedness and have included ambidextrous subjects into left-handedness group (Medland et al., 2003; Neale, 1988). Our data suggest that most subjects who classify themselves as ambidextrous should be combined with right-handed subjects, at least when handedness is defined as a writing hand; almost all (96.5%) of the ambidextrous subjects who were not forced to use their right hand were nonetheless right-handed writers in adulthood. This argues strongly against the view that ambidextrous persons are more likely to become left-handed writers if no cultural pressure exists. Of course our definition of ambidextrousness was based on a single question, and thus it might not capture the complexity of ambidextrousness; but we note that three of the six ambidextrous subjects at age 14 in our FinnTwin12 sample were categorized as ambidextrous as young adults and the other three subjects were almost totally right-handed as measured with the EHI. It is also possible that people understand childhood handedness in different ways. We have shown that whether ambidextrous subjects are classified into left- or right-handers has a small effect on the genetic analyses.

4.2. Sex differences in handedness

When it comes to sex differences, in support of earlier studies, we found that males were more likely to be left-handed, and further that difference was evident in singletons, twins and triplets separately. Even if the prevalence of left-handedness was little lower than expected, the sex difference of about 2% was comparable to other studies (Gilbert & Wysocki, 1992; Ooki, 2005; Peters et al., 2006). However, the genetic component to handedness did not differ by sex.

4.3. Handedness prevalence in singletons, twins and triplets

In contrast to the earlier study by Medland et al. (2003), we found increased prevalence of left-handedness in twins compared to singletons. An earlier meta-analysis indicated that twins

display higher incidence of left-handedness than singletons (Sicotte et al., 1999). Also, one study found twins and triplets, born between 1960–66, were twice as likely as singletons to be left-handed (Williams et al., 1992). One possible factor that can explain the higher incidence of left-handedness in twins could be the smaller birthweight in twins than in singletons. Twins are born about 1 kg lighter at birth than singletons, due primarily to gestation (Loos, Derom, Derom, & Vlietinck, 2005). At least in singletons, very low birthweight has been associated with non-right-handedness (Powls, Botting, Cooke, & Marlow, 1996; Saigal, Rosenbaum, Szatmari, & Hoult, 1992); thus, the observed difference in prevalence of left-handedness between twins and singletons might in part have arisen from the lower average birthweight of twins. Twins and triplets might be also at elevated risk for pregnancy and birth related complications, at least in our sample where all subjects were born before 1958, which can also be associated with left-handedness. For example, infant resuscitation (Williams et al., 1992) and maternal age are related to left-handedness (Bailey & McKeever, 2004). We also found that triplets were more likely to be ambidextrous, which can also be related to birth and pregnancy complications. It can be speculated as well that increased left-handedness in twins and triplets compared to singletons, and also increased number of ambidextrousness in triplets compared to twins and singletons could be at least partly related to uterine position of the fetus. As reviewed by Previc (1991) in singletons, most fetuses have their right ear and hand towards the outside world during the third trimester. The typical uterine position of a fetus during the end of the pregnancy can also be caused by the earlier formation of handedness, which possibly takes places already during the first trimester (Hepper et al., 1998).

4.4. Handedness in twins

Although the effect of birth order has been reported to be related to handedness in twins (James & Orlebeke, 2002) our results do not support this and are in line with the results of Medland et al. (2003). Nor did we have any evidence from mirror imaging of MZ twins. If mirror imaging were to affect handedness, it would be seen in the higher rate of left-handedness in MZ twins, which was not the case in our study. Similarly, one study (Derom, Thiery, Vlietinck, Loos, & Derom, 1996) found no evidence of association between handedness and placentation or zygosity type. Although individual cases of mirror imaging twins with discordant handedness have been reported (Sommer, Ramsey, Bouma, & Kahn, 1999; Sommer, Ramsey, Mandl, & Kahn, 2002) discordant handedness in MZ twin pairs does not represent mirror imaging phenomenon in general.

4.4.1. Genetic and environmental effects in handedness—Our genetic modelling indicated that unique environmental effects explain most of the variance, both in childhood and adult handedness, although there are modest familial effects, as well. Although we have one of the largest twin data sets on which the handedness has been studied to date, we cannot conclude whether the familial effects in adult writing handedness are additive genetic or common environmental effects, because both AE and CE models fit the data. For current writing hand a full ACE model fitted the data, as well, but there was little power to detect the common environmental effects. If common environmental effects account for but 1–2% of the variance, larger data sets would be needed to detect such effect. In childhood handedness, when ambidextrous subjects were combined with right-handed subjects, the best fitted model indicated that the familial effects are additive genetic effects. The division right-handed/ambidextrous versus left-handed subjects is justified by the fact that almost all ambidextrous subjects, who were not forced use their right hand, do write with their right hand. Instead, when ambidextrous subjects were combined with left-handed subjects additive genetic effects accounted only for 2% of the variance. Regarding estimated heritability for the writing hand, our results are in line with the recent meta-analysis (Medland et al., 2006) which indicated that 25% of the variance in handedness is accounted by additive genetic effects while most the variance is accounted by unique environmental effects. In a model where forced right-

handedness was taken into account, our equivalent numbers were 26% and 74% for additive genetic and unique environmental effects, respectively. Alternatively a CE model, which also fitted our data in writing hand, yielded 18% of the variance explained by common environmental effects and 82% of the variance explained by unique environmental effects. This in turn, is in line with the previously second largest twin study on handedness (Medland et al., 2003), where variance in writing-hand was accounted by common environmental (12%) and unique environmental (88%) effects. In the study by Medland et al. (2003) they also used throwing hand, which was explained by additive genetic (27%) and unique environmental effects (73%). Interestingly they have used the throwing hand data, but not writing hand, in their meta-analysis (Medland et al., 2006). The most recent study of genetic effects on handedness with over 54 000 subjects from over 25 000 Australian and Dutch families, indicated that genetic effects accounted for 25% of the variance (Medland et al., 2008). This result is in line with our study, even if the prevalence of left-handedness was much higher than in our sample: 12.5% in females and 14.6% in males in the Australian sample, and 15.2% in females and 17.6% in males in the Dutch sample.

We have demonstrated that taking forced handedness into account increases the magnitude of familial effects evident in model-fitting. This is important especially when dealing with older cohorts; nowadays this probably is not a problem, since attitudes towards left-handedness are more permissive, at least in western cultures. Even if we were not able to perform the model-fitting for different age groups separately due to small number of left-handed concordant pairs, the age effect was partly controlled when we performed the model-fitting where we did not include the persons who were forced to use their right hand. But as the prevalence of left-handedness decreased also in those subjects who were not forced to use their right hand we cannot draw conclusions whether the genetic effects are of same magnitude in different cohorts.

Some earlier twin studies have not found any familial effects in handedness which has been due to lack of power to detect any genetic or common environmental effects. Left-handed concordant twin pairs are rare, and thus very large samples are needed to detect any familial effects in handedness. The recent genetic mapping studies of handedness have yielded support to a genetic basis of handedness (Francks et al., 2002; Medland et al., 2005; Van Agtmael, Forrest, & Williamson, 2002). Handedness measured with hand skill has been associated with LRRTM1 gene on chromosome 2p12 in dyslectics (Francks et al., 2007). There are also some results from non clinical populations. The writing hand has been linked to androgen receptor length (Medland et al., 2005) and also to chromosome 12q21-23 (Warren, Stern, Duggirala, Dyer, & Almasy, 2006). Handedness measured with Edinburgh Handedness Inventory has shown a linkage on chromosome 10q26 (Van Agtmael et al., 2002). These studies clearly demonstrate that genes play some role in the formation of handedness and they strongly argue against monogenic theories of handedness. Although genetic variation is related to handedness, a remarkable proportion of variance in handedness is explained by environmental effects. In conjunction with genetic studies of handedness, these possible environmental factors should be examined before we can understand the formation of human handedness. It is still unclear what environmental effects can cause the selection of dominant hemisphere with relation to handedness. One possible source could be the complementary roles of the arms/hemispheres during motor performance. As reviewed by Goble and Brown (2008), trajectory control and visual feedback for movement is processed more accurately with the preferred arm/dominant hemisphere while positional control and proprioceptive feedback is utilized more accurately with the non-preferred arm/non-dominant hemisphere. This specialization of the arms is most likely based on the anatomical differences of the hemispheres in the motor systems. The pre-existing asymmetry in motor cortex, usually greater connectivity of motor cortex in left hemisphere, could function as the foundation of handedness. As reviewed by Hammond (2002) the motor cortex has extensive interconnections and has therefore experience-based potential for functional reorganization. So, typically, the anatomical asymmetry would lead to

increased practise of the dominant (usually right hand), and thus further enhance the dexterity of that dominant hand. Thereby, living in a society, which strongly favours the use of right hand, could encourage enhanced use of right and left hand for trajectory and positional control, respectively, thus masking the potential genetic background for possible reversed asymmetry of motor cortex. While in societies, which are permissive in terms of handedness, the individual experiences could lead to greater variation in handedness. Besides the genetic effects, the reasons for the lack of pre-existing advantage of the greater connectivity of motor cortex in left hemisphere could include biological (e.g. lesion) and hormonal (e.g. uterine hormonal environment) effects. Taken together the fact that most of the variance in handedness is explained by environmental effects unique to each individual, and that there exists a general bias for right-handedness in humans it seems that while there is pre-existing asymmetry in motor systems in favour of right hand use, the right hemisphere functions as a reserve when reorganization of motor cortex is needed. In future research, it would be useful to conduct twin studies of arm preference for trajectory/positional control and for visual/proprioceptive feedback processing to see whether the complementary roles of the arms are of genetic or environmental origin.

4.5. Limitations

Our study has some limitations. Our question concerning childhood handedness may be prone to retrospective reporting errors. Especially in older subjects the validity of the childhood handedness report can be questioned. Similarly, answering a forced handedness question may be susceptible to recall errors. It is possible that in the beginning of the 20th century there has been a general atmosphere for encouraging the use of right hand instead of left, thus resulting in smaller than expected prevalence of left-handedness in our sample. Another limitation of our study was that we did not have birthweight information from our subjects. It is possible that the higher prevalence of left-handedness in twins and triplets compared to singletons could, at least in part, be due to lower birthweight. Finally, the prevalence of left hand concordant twin pairs was very low, and we could not conclude whether the familial effects we observed are genetic or environmental, even though we had one of the largest individual twin data sets in which handedness has been studied.

4.6. Conclusion

To conclude, we have demonstrated that ambidextrous subjects are more likely to become right hand writers when there is no pressure for using the right hand. We have also shown that most of the variance in handedness is explained by environmental effects, while there are also some familial, probably genetic effects that are not detectable in smaller samples.

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Fig. 1. Path diagram for univariate model illustrating additive (A), common environmental (C), and unique environmental (E) correlations between monozygotic (MZ) and dizygotic (DZ) twins.

Fig. 2. Scatter plot of the relationship between handedness at age 14 and laterality quotient (LQ) at age 21–24 among 532 twin individuals.

Table 1
Frequencies of childhood handedness and adult writing hand (% and n of subjects)

	Singletons	Twins	Triplets	All subjects
Handedness as a child				
Right-handed	90.7% (3688)	88.5% (22847)	86.6% (245)	88.8% (26780)
Left-handed	5.8% (234)	8.1% (2085)	7.1% (20)	7.8% (2339)
Ambidextrous	3.5% (142)	3.4% (873)	6.4% (18)	3.4% (1033)
Adult writing hand				
Left	4.5% (183)	6.1% (1563)	6.4% (18)	5.9% (1764)
Right	95.5% (3879)	93.9% (24236)	93.6% (264)	94.1% (28379)

Table 2

Stability of handedness in all subjects from childhood to adulthood

	Not forced to use right-hand		Forced to use right-hand	
	Adult			
Child	L	R	L	R
R	1.6% (417)	98.4% (25756)	8.4% (19)	91.6% (207)
L	73.5% (884)	26.5% (318)	34.3% (388)	65.7% (744)
A	3.5% (28)	96.5% (773)	5.5% (12)	94.5% (207)

R = right-handed, L = left-handed, A = ambidextrous

Table 3

Stability of handedness in twins from childhood to adulthood

Child	Not forced to use right-hand		Forced to use right-hand	
	Adult			
	L	R	L	R
R	1.6% (358)	98.4% (22238)	9.4% (18)	90.6% (173)
L	73.6% (790)	26.4% (284)	35.3% (355)	64.7% (652)
A	3.2% (22)	96.8% (663)	6.1% (11)	93.9% (168)

R = right-handed, L = left-handed, A = ambidextrous.

Note. The groups in bold cases are included in the genetic models, where the handedness has been controlled.

Table 4

The proportion of left-handedness, ambidextrousness and forced right-handedness in different age groups

Age	Childhood left-handedness	Childhood ambidextrousness	Adult left-handed writers	Forced right-handers within left-handers
18–19	8.8%	2.8%	8.8%	20.9%
20–29	8.5%	2.9%	7.5%	39.1%
30–39	7.2%	3.3%	5.6%	51.2%
40–49	7.1%	4.2%	3.8%	71.4%
50–59	6.9%	4.3%	3.0%	70.2%
60–69	6.9%	4.8%	3.0%	60.3%

Table 5
Pairwise childhood handedness for monozygotic (MZ) and dizygotic (DZ) twin pairs

	Twin 2		
	Right-handed	Left-handed	Ambidextrous
MZ twins			
Twin 1			
Right-handed	2726	222	80
Left-handed	246	35	6
Ambidextrous	91	4	9
DZ twins			
Right-handed	5803	540	237
Left-handed	534	40	15
Ambidextrous	220	10	12

Table 6
Pairwise writing handedness for monozygotic (MZ) and dizygotic (DZ) twin pairs
after controlling for forced handedness

		Twin 2	
		Right-handed	Left-handed
MZ twins			
	Twin 1		
	Right-handed	2740	124
	Left-handed	154	21
DZ twins			
	Right-handed	5888	310
	Left-handed	280	27

Table 7
Univariate genetic model fitting statistics for childhood and current writing handedness

	Model	df	X ²	AIC	A (CI)	C (CI)	E (CI)
Childhood handedness	R vs. L	4	8.05	0.05	7% (0–15%)	-	93% (85–100%)
	CE	4	10.05	2.05	-	2% (0–8%)	98% (92–100%)
	E	5	10.38	0.38	-	-	100%
	R vs. L/A	4	12.87	4.87	2% (0–9%)	-	98% (91–100%)
	CE	4	13.15	5.15	-	0% (0–4%)	100% (96–100%)
	E	5	13.15	3.15	-	-	100%
	R/A vs. L	3	7.69	1.69	8% (0–16%)	0% (0–6%)	92% (84–100%)
	AE	4	7.69	-0.31	8% (0–16%)	-	92% (84–100%)
	CE	4	10.04	2.04	-	3% (0–9%)	97% (91–100%)
Current writing hand	R vs. L	5	10.67	0.67	-	-	100%
	Not controlled	3	3.76	-2.24	19% (0–30%)	1% (0–19%)	80% (70–91%)
	AE	4	3.77	-4.23	21% (11–30%)	-	79% (70–89%)
	CE	4	5.52	-2.48	-	14% (7–21%)	86% (79–93%)
	Controlled	3	5.57	-0.43	24% (0–37%)	2% (0–23%)	74% (63–87%)
	AE	4	5.58	-2.42	26% (16–37%)	-	74% (63–84%)
	CE	4	7.79	-0.21	-	18% (10–26%)	82% (74–90%)

Note. R = right-handed, L = left-handed, A = ambidextrous

AIC = Akaike's information criterion

A = additive genetic effects, C = common environmental effects, E = unique environmental effects

CI = Confidence Intervals

Not controlled = All subjects included

Controlled = Analysis restricted to those groups shown in bold in Table 3.