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Non-right-handedness and mental health problems among adolescents from the general population: The Trails Study

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ABSTRACT

To determine whether the association between non-right-handedness and mental problems among adolescents is specific for psychotic symptoms, we included a group of 2096 adolescents with a mean age of 14 years from the general population. Mental health problems were assessed using the parent, self-report, and teacher versions of the Child Behavior Checklist. Internalising problems comprised anxious and depressed, withdrawn and depressed, and somatic complaints. Externalising problems consisted of delinquent behaviour and aggressive behaviour. The remaining problems consisted of social problems, attention problems, and thought problems. The latter were divided into psychotic and non-psychotic items. A total of 14.3% of the adolescents were non-right-handed. We observed positive associations of non-right-handedness with thought problems, social problems, and being withdrawn and depressed. Externalising problems showed no associations with handedness. Within the thought problems subscale, the effect sizes associated with non-right-handedness for psychotic and non-psychotic items were 0.18 ($p=.005$) and 0.04 ($p=.459$), respectively. In conclusion, non-right-handedness is predominantly associated with psychosis-related mental problems as early as in adolescence. Handedness could be taken into account when identifying adolescents at risk for psychosis.

INTRODUCTION

Approximately 10% of the general population is non-right-handed (Perelle & Ehrman, 2005), with a slight overrepresentation of males (Peters & Pedersen, 1978). Non-right-handedness, including mixed handedness, is associated with psychiatric disorders such as autism and borderline personality disorder (Dane & Balci, 2007; Niederhofer, 2004), as well as neurological disorders (Aygu" l, Dane, & Ulvi, 2005), and mortality in women (Ramadhani et al., 2007). However, the predominant association with non-right-handedness was found for adult patients diagnosed with schizophrenia (DeLisi et al., 2002; Dragovic & Hammond, 2005; Sommer, Aleman, Ramsey, Bouma, & Kahn, 2001), first shown by Gur (1977). Non-right-handedness is of scientific interest because it is a marker of atypical cerebral lateralisation of functions that, in turn, is considered a potential risk factor for schizophrenia (Crow, Done, & Sacker, 1996; Sommer et al., 2001).

Schizophrenia comprises various mental health symptoms, but in particular psychotic symptoms such as social withdrawal and thought problems. There is substantial evidence that schizophrenia represents the extreme of a psychosis continuum rather than a discrete disease entity (Johns & van Os, 2001). Whether the association of non-right-handedness with clinical schizophrenia can be generalised to a psychosis continuum in the general population is largely unknown. Research among present-day adolescents is of specific interest as this age group has not been forced to write right-handed, which itself may be associated with slower performance and thereby poorer mental health (Chen & Su, 2006).

It can be hypothesised that non-right-handed individuals may have more mental problems than right-handed people, rather than specifically more psychotic symptoms. Demonstration of specificity of non-right-handedness for psychotic symptoms makes a biological mechanism more likely than any other mechanism such as social pressure against left-handedness. To that end, it is necessary to measure a

range of mental health problems. No previous studies on handedness and psychopathology have addressed the question of specificity.

The underlying cause of the association of schizophrenia with non-righthandedness is unknown. It is suggested that non-right-handedness is a marker of failure to lateralise, which in turn plays a role in the development of schizophrenia as well as in poorer verbal and spatial ability (Crow, Crow, Done, & Leask, 1998; Leask & Crow, 2005; Peters, Reimers, & Manning, 2006). Non-right-handedness may also be promoted by damage to the left hemisphere as a result of obstetric factors (Basso, 2007). As hypoxic obstetric complications have been associated with schizophrenia (DeLisi et al., 2002; Dragovic & Hammond, 2005; Sommer et al., 2001), they may constitute a common cause of both schizophrenia and non-righthandedness. However, the contribution of obstetric complications to the development of schizophrenia and psychosis is uncertain, as some studies have shown no relationship at all (Cannon, Jones, & Murray, 2002; Done et al., 1991).

In the present study we investigated handedness in relation to a range of mental problems among adolescents from the general population. We hypothesised that non-right-handedness is specifically associated with psychotic problems, rather than with mental health problems in general. We additionally hypothesised that the associations are, at least in part, explained by obstetric factors related to hypoxia.

METHODS

Sample

The TRacking Adolescents' Individual Lives Survey (TRAILS). TRAILS is a prospective cohort study of Dutch (pre)adolescents, with the aim of charting and explaining the development of mental health from preadolescence into adulthood. The present study involves data from the first (T1) and second

(T2) assessment wave of TRAILS, which ran from March 2001 to July 2002, and September 2003 to December 2004, respectively.

Sample selection.

Five municipalities in the north of the Netherlands, including both urban and rural areas, were requested to provide names and addresses of all inhabitants born between 10-01-1989 and 09-30-1990 (first two municipalities) or 10-01-1990 and 09-30-1991 (last three municipalities), yielding 3483 names. Simultaneously primary schools, including schools for special education, within these municipalities were approached with the request to participate in TRAILS. School participation was a prerequisite for eligible children and their parents to be approached by the TRAILS staff, with the exception of those already attending secondary schools (81%), who were contacted without involving their schools. Of the 135 primary schools within the municipalities, 122 (90.4% of the schools accommodating 90.3% of the children) agreed to participate in the study. Children were excluded from the study if they were incapable of participating due to mental retardation or a serious physical illness or handicap, or if no Dutch-speaking parent or parent surrogate was available and it was not feasible to administer any of the measurements in the parent's language. This resulted in exclusion of 6.7% of all children approached for enrolment in the study (N3145). Of the remaining 2935 children, 76.0% (N=2230) were enrolled in the study (Huisman et al., 2008). Of the 2230 baseline participants, 96.4% (N=2149) participated in the first follow-up assessment (T2), which was held 23 years after T1 (mean number of months 29.4, SD=5.4, range 16.7-48.1). Mean age at T2 was 13.6 (SD=0.5). Responders and non-responders did not differ with respect to the prevalence of teacher-rated problem behaviour, nor regarding associations between sociodemographic variables and mental health outcomes (De Winter et al., 2005).

Measures

Data collection. At T1, well-trained interviewers visited one of the parents or guardians (preferably the mother, 95.6%) at their homes to administer an interview covering a wide range of topics, including developmental history and somatic health, parental psychopathology, and care utilisation. Besides the interview, the parent was asked to fill out a self-report questionnaire. Children filled out questionnaires at school, in the classroom, under the supervision of one or more TRAILS assistants. Teachers were asked to fill out a brief questionnaire for all TRAILS children in their class. T2 involved only questionnaires, to be filled out by the children (adolescents now), their parents, and their teachers. As in T1, the adolescents completed their questionnaires at school. Measures that were used in the present study are described more extensively below.

General characteristics.

Participants were asked about their handedness in a questionnaire about general health at T1. The question put was: “What is the hand you are writing with?” and possible answers were “left”, “right”, or “alternating”.

Mental health problems.

Mental health problems were assessed by the adolescents themselves, their parents, and their teachers. The Child Behaviour Checklist (CBCL) and the Youth Self-Report (YSR) were filled out by the parents and adolescents, respectively (Verhulst & Achenbach, 1995). Both instruments comprise a set of 120 emotional and behavioural questions regarding the past 6 months, to be scored as follows: 0=not true, 1=somewhat or sometimes true, 2=very true or often true. These questionnaires are frequently used in current child and adolescent psychiatric research (Verhulst & Achenbach, 1995). The questionnaire filled out by the teachers was the Teacher’s Checklist of Psychopathology based on the Teacher Report Form (De Winter et al., 2005). It contains nine questions corresponding to CBCL/YSR syndrome scales, which can be rated from 0=not applicable to 4=very clearly or frequently applicable, or 5=almost always applicable in the last 2 months.

Due to the age-related increase in incidence of clinically manifest psychosis during adolescence, we expected a higher level of psychotic symptoms at T2 than at T1. So prior to the analysis we decided to use T2 rather than T1 mental health data.

We calculated a combined estimate of mental health using the scores given by the different informants. Information from multiple sources, rather than from a single source, is a better predictor of disorder and it is the best estimate of diagnosis for individual cases as it reduces rater bias in the prediction of mental health outcomes (Verhulst, Koot, & Van der Ende, 1994). To weigh information from different informants equally, the scores on YSR, CBCL, and TCP were all standardised to a 0 to 1 scale by dividing the scores on each scale by its range before averaging over informants. Using data from these instruments we constructed a broad-band domain internalising problems comprising anxious/depressed, withdrawn/depressed, and somatic problems, as well as a broad-band domain externalising problems comprising aggressive behaviour and delinquent behaviour. The remainder sub-domains were: thought problems, attention problems, and social problems. We divided the items in the thought problems scale into psychotic and non-psychotic items, prior to the analyses. Items considered indicative of psychotic thought were: "I hear sounds or voices that are not there according to other people", "I see things that are not there according to other people", and "I have thoughts that other people consider strange or absurd".

Obstetric factors.

Obstetric factors were assessed using a questionnaire filled out by one of the parents, usually the mother, at T1. Obstetric factors included pregnancy duration, birth weight, the need for a Caesarean section, the use of vacuum or forceps assisted birth, neonatal oxygen treatment, nursing in an incubator, and the influence of nicotine during pregnancy.

Data analysis

Differences in general characteristics and obstetric factors between the handedness groups were tested for statistical significance using the two-tailed t-test for continuous variables and Mann-Witney U test for categorical variables. Multiple linear regression models were used to quantify the association between handedness as the independent variable and the various mental health problems as the dependent variables, adjusted for gender. We checked the assumptions of multiple linear regression including linearity, homoscedasticity, and normality of the outcome variables as well as the fit of the models using scatter and residual plots. We also investigated whether any association between handedness and mental health problems could be explained through obstetric factors, by assessing to what extent the coefficient for handedness in the regression model changed when adding the obstetric variables as covariates. The effect size associated with nonright-handedness was calculated by dividing its regression coefficient by the standard deviation of the dependent variable. Data analyses were performed with SPSS, version 14.0 for Windows.

RESULTS

In total, 2096 participants were included in the present analysis. Table 1 shows their demographic and obstetric characteristics. There were 300 (14.3%) non-right-handed adolescents. Of these, 24 (1.1%) were mixed-handed and 276 (13.2%) were left-handed. Age was similarly distributed across both groups. Although there were no significant differences in the assessed obstetric factors between right-handed and non-right-handed adolescents, there was a trend towards more obstetric complications in the non-right-handed group, with the exception of maternal smoking, which was more prevalent in the right-handed group.

Handedness in association with internalising, externalising, and remaining problems, i.e., social, attention and thought problems, is presented in Table 2. In general, mental health problems tended to be more severe in non-right-handed than in right-handed adolescents, with the exception of

externalising problems Overall, internalising problems were significantly more common in non-right-handed participants. Within this category, the dimension withdrawn and depressed was mainly responsible for this difference, with an effect size of 0.17. The other dimensions were not statistically related to handedness; however the measured effects, though not significant, were consistently in the same direction. In the externalising category the associations with handedness were reversed, very small, and statistically not significant. For the last category, that of remainder problems -social, attention, and thought problems- differences in the levels of mental health problems between right- and non-right-handed adolescents were the most pronounced. Within this category, levels of social as well as thought problems differed substantially between groups, with effect sizes of 0.18 and 0.16 respectively, again to the disadvantage of the non-right-handed group. Adjusting for gender had no material effect on the results. Including the obstetric variables in the regression models did not affect the estimates for handedness either. This indicates that the associations of handedness with mental problems were largely independent of the obstetric factors measured. For these results we used T2 data. Nevertheless, when we redid the analyses using T1 data, the same patterns emerged.

Thought problems subscale

We divided the thought problems subscale into psychotic and non-psychotic items. To the psychotic item "hearing noises and voices that others do not hear", 6.7% of the adolescents answered "little or sometimes" and 1.7% answered "clearly or often". To the item "seeing things that others do not see", 5.0% gave the answer "little or sometimes" and 1.3% answered "clearly or often". To "having strange thoughts", 10.2% of the adolescents answered "little or sometimes" and 1.9% "clearly or often". Table 3 shows the levels of thought problems separately for the psychotic and the non-psychotic items. Whereas the psychotic items were strongly associated with non-right-handedness, non-psychotic items were not. The effect size of the association of psychotic items with non-right-handedness was 0.18. Within this group, the largest and statistically significant effects were observed for "Having strange

thoughts” and “seeing things that others do not see”. Use of oxygen as a neonate was the only obstetric factor that was associated with a higher score on the psychotic items (mean difference=0.033, 95% CI=0.0070.058, effect size=0.21). Adjusting the association of handedness by the psychotic item for each obstetric factor, did not alter the association.

DISCUSSION

In summary, in the present study we observed a substantial positive association of non-right-handedness with thought problems, social problems, and being withdrawn and depressed in adolescents from the general population. Within the thought problems subscale, the associations related solely to the psychotic items. There was virtually no association of non-righthandedness with the non-psychotic items. Obstetric factors could not explain these associations, as we did not see an association of handedness and obstetric factors. Externalising problems showed no associations with handedness.

Before we interpret our findings, some potential limitations must be addressed. Obstetric factors were assessed by a questionnaire usually filled out by the mother over 10 years after the fact. This may have resulted in some misclassification of the obstetric factors due to recall errors and some possible differences between questionnaires filled in by fathers in contrast to mothers. It is, however, unlikely that this has a meaningful effect on the data, as the questions related mostly to quite severe events that were not likely to be reported wrongly, either false positively or false negatively. Moreover, it is almost inconceivable that recall errors depended on both children’s handedness and their present mental health problems. Consequently, bias due to systematic error in recall of obstetric factors is highly unlikely. Other studies have shown associations between obstetric factors and handedness; however, in most previous studies on handedness and schizophrenia, older adults who might have been forced to switch handedness were included (Basso, 2007; Perelle & Ehrman, 2005). This could have caused psychological stress, which might have promoted unfavourable mental health outcomes.

In our investigation among adolescents carried out between 2001 and 2004 this form of bias cannot have occurred, as social pressure related to handedness has largely disappeared over the past decades. The group of adolescents who classified themselves as non-right-handed consisted of a group of left-handed and mixed-handed adolescents. Due to the limited number of mixed-handed participants we were unable to distinguish between associations of psychopathology with mixed-handedness and with left-handedness. Because the mixed-handed group was very small, the results mainly reflect the effect of left-handedness.

Our study has several strong points: the large sample size, the source of the study population (i.e., from the general population), and the extensive measurement of mental health on a continuous scale using information from multiple informants. In addition we assessed a broad range of mental health problems, allowing us to determine whether associations with handedness were specific for certain problems, in particular for psychotic symptoms.

The assessment of hand preference was relatively simple. However, the distribution of hand preferences in our study population with a large proportion of non-right-handedness was remarkably similar to the distribution in a similarly aged group from the BBC Internet Study (Peters et al., 2006). Previously, by far the most studies on handedness and psychopathology were done in adulthood. A meta-analysis of 16 cross-sectional studies on handedness and schizophrenia showed that non-right-handedness is significantly more prevalent in patients with schizophrenia than in healthy participants (Satz & Green, 1999; Sommer et al., 2001). Also the personality trait schizotypy, an attenuated, sub-clinical expression of the psychosis phenotype in schizophrenia, has been associated in adults with one or both types of non-right-handedness (Poreh, Levin, Teves, & States, 1997; Preti, Sardu, & Piga, 2007). As far as we know, only one study has been conducted on handedness and a continuous psychosis dimension among adolescents (Chen & Su, 2006). Chen and Su showed more non-right-handedness in youngsters with higher levels of schizotypy in a group of adolescents of mean age 14 (Chen & Su, 2006).

However, in this relatively small study of 118 adolescents, associations with specific items like auditory and visual hallucinations and obstetric factors were not reported. Moreover, they did not address the question of whether associations were specific for schizotypal features or mental problems in general.

To explain our findings it is of specific importance to realise that two main features of schizophrenia are social withdrawal and thought problems, and that sub-clinical psychosis in childhood is associated with schizophrenia in adult life (Poulton et al., 2000). The association of non-right-handedness with predominantly these problems at a sub-clinical level is thus intriguing and supportive of an association of handedness with a continuum of psychosis (Chen & Su, 2006). Taking a closer look at the internalising problems and the association with non-right-handedness shows that the “withdrawn/depressed” scale was largely driven by an association with being withdrawn. This in turn mainly caused the significant association with the total internalising problems scale. The observation that within the thought problems domain the psychotic items were specifically associated with nonright-handedness further supports our hypothesis that the association is specific, rather than generic.

Our findings suggest that atypical cerebral lateralisation may be a specific risk factor for an upward shift in the psychosis continuum in the general population. It has been suggested that both non-right-handedness and schizophrenia may be due to a lack of oxygen as a result of obstetric complications. Whether they constitute a common pathway is a matter of debate, as positive and negative findings are present (Crow, 2008; Done et al., 1991) and problems exist regarding current approaches (Cannon et al., 2002). However, it is also supported by the results from both animal (Tejkalova´, Kaiser, Klaschka, & Sˇtasny´, 2007) and human (Cannon et al., 2002) studies. The results of the latter study are in line with our results, showing an association between psychosis-related items and neonatal oxygen treatment. However, because obstetric factors were not associated with handedness in our study they

could not explain the associations with mental problems. Our finding of no relationship between handedness and obstetric factors is consistent with the conclusion of a meta-analysis (Searleman, Porac, & Coren, 1989). Our results, showing that non-right-handed adolescents do not generically have poorer mental health, refute the theory that social pressure against non-right-handedness rather than non-right-handedness itself is the origin of the association. We also studied associations between handedness and mental health problems by informant, i.e., adolescents themselves, parents, and teachers. We were particularly interested in the expected differences between teacher ratings and those of other informants, because it has been shown that teachers report left-handed children as having poorer speech and writing abilities but we could not confirm these results (Basso, 2007). Interestingly, our findings showed the same trends irrespective of informant.

There may be clinical implications to our study. In a meta-analysis of 21 controlled studies it was shown that early treatment of schizophrenia results in better outcomes (Killackey & Yung, 2007). If handedness is associated with schizophrenia independently of other risk factors for psychosis, such as family history, it could be of aid in the identification of a high-risk group of clinical psychosis, which might benefit from receiving lifestyle advice, such as to refrain from using cannabis, or they might be intervened upon otherwise. Interestingly, a recent meta-analysis shows promising results for intervention during the prodromal phase of schizophrenia (Gleeson, Larsen, & McGorry, 2003).

CONCLUSION

In conclusion, our observations suggest that non-right-handedness is associated with mental health problems in adolescents from the general population, particularly with psychosis-related problems. Our findings do not support the hypothesis that the association between mental problems and non-right-handedness is explained by obstetric factors.

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest. This research is part of the TRacking Adolescents' Individual Lives Survey (TRAILS). Participating centres of TRAILS include various departments of the University Medical Centre and University of Groningen, the Erasmus University Medical Centre Rotterdam, the University of Utrecht, the Radboud Medical Centre Nijmegen, and the Trimbos Institute, all located in the Netherlands. Principal investigators are Prof. Dr J. Ormel (University Medical Centre Groningen) and Prof. Dr F. C. Verhulst (Erasmus University Medical Centre). We are grateful to all adolescents, their parents and teachers who participated in this research and to everyone who worked on this project and made it possible.

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TABLE 1 - General and obstetric characteristics based on present handedness

	Non-right	Right	p-value
	N=300 (14.3%)	N=1796 (85.7%)	
Age (years), mean (SD)	13.6(0.51)	13.6(0.53)	0.678
Male gender (%):	54.3	47.8	0.037
Pregnancy duration (weeks), mean (SD)	39.8(1.9)	39.8(2.0)	0.897
Birth weight (gram), mean (SD)	3353(617)	3402(619)	0.205
Caesarean section (%)	6.7	8.0	0.466
Vacuum or forceps assisted birth (%)	9.8	9.4	0.855
Treated with oxygen as a neonate (%)	3.0	2.3	0.420
Treated in an incubator as a neonate (%)	8.4	7.3	0.515
Smoking (%)	27.6	30.6	0.311

N=2096.

TABLE 2 - Handedness associated with mental health problems

Mental health outcome	Difference (95% CI)**	p-value	Effect size
Internalising problems	0.015(0.001–0.028)	0.029	0.14
Anxious and depressed	0.012(–0.003–0.028)	0.108	0.09
Withdrawn and depressed	0.024(0.007–0.042)	0.006	0.17
Somatic complaints	0.007(–0.008–0.022)	0.376	0.06
Externalising problems	0.003(–0.017–0.011)	0.677	–0.03
Aggressive behaviour	0.001(–0.016–0.017)	0.949	0.01
Delinquent behaviour	0.007(–0.020–0.007)	0.353	–0.06
Remaining problems	0.018(0.004–0.032)	0.011	0.16
Social problems	0.025(0.008–0.042)	0.004	0.18
Attention problems	0.011(–0.009–0.031)	0.284	0.07
Thought problems	0.018(0.005–0.031)	0.008	0.16
Total problems	0.011(0.000–0.023)	0.053	0.12

N=2096 adjusted for gender. **Difference in mental health problems with values greater than zero indicating higher levels in non-right-handed than in right-handed adolescents.

TABLE 3 - Handedness associated with psychotic items of the thought problems

Thought problem scale outcome	Difference (95%CI)**	p-value	Effect size
Psychotic items	0.047(0.014–0.080)	0.005	0.18
Hearing noises and voices that others do not hear	0.021(-0.023–0.065)	0.349	0.06
Seeing things that others do not see	0.044(0.006–0.083)	0.024	0.14
Having strange thoughts	0.080(0.031–0.129)	0.001	0.20
Non-psychotic items	0.012(-0.020–0.045)	0.459	0.04

N=2048 adjusted for gender. **Difference in mental health problems with values greater than zero meaning higher levels in non-right-handed than in right-handed adolescents.