

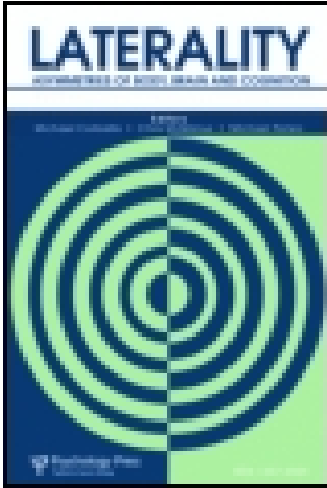
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Psychiatric disorders and left-handedness in children living in an urban environment

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The objective of this study was to conduct an analysis of left-handed children treated in an urban mental health clinic to investigate the frequency and severity of psychiatric disorders compared to right-handed peers. Data on handedness, diagnoses, hospitalizations and severity of mental disorders were collected on 692 consecutive children, 4–18 years old ($M = 10.1$, $SD = 3.2$), referred for psychiatric evaluation. Left-handed children were 18.2% of patients in the study, a rate significantly higher than left-hand dominance in the USA ($p < .05$). Compared to children with right-handedness, logistic regression analysis yielded 31% [odds ratio (OR) = 1.31, 95% confidence interval (CI): 1.15–1.50] higher odds of having more psychiatric diagnosis, 70% (OR = 1.70, 95% CI: 1.10–2.62) increased odds of anxiety, 53% (OR = 1.53, 95% CI: 1.03–2.27) increased odds of depression and 78% (OR = 1.78, 95% CI: 1.21–2.62) increased odds of oppositional defiant disorder for children who were left-handed. Left-handed children had increased odds of being prescribed antipsychotic and anxiolytic medication uses, 53% and 86% increased odds, respectively, and 66% (OR = 1.66, 95% CI: 1.08–2.55) increased odds of psychiatric hospitalizations. Left-handedness was a phenotypic risk factor for psychiatric disorders and increased severity of psychiatric disorders.

Keywords: Handedness; Childhood; Psychiatric disorders; Oppositional disorder.

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There are few phenotypic traits associated with psychiatric disorders. One such trait, left-handedness, occurs in 11.1% of the US population (Gilbert & Wysocki, 1992). Left-handedness clusters in familial lineages (McKeever, 2000) and is related to higher rates of depression, schizophrenia and bipolar disorders in adults (Bellani et al., 2010; Denny, 2009; Leask & Crow, 2005; Nowakowska et al., 2008). Studies of left-handedness and psychiatric disorders in childhood are rare, especially in urban populations. One recent population-based study of children in the Netherlands documented an association between left-handedness and behaviour disorders (van der Hoorn et al., 2010). Non-right-handed children in the Netherlands study had higher rates of behaviour problems on parent, self and teacher reports.

The high rate of left-handedness observed in epidemiological studies of adults with psychiatric disorders promoted genetic linkage studies to identify markers underlying the association between left-handedness and schizophrenia and affective disorders. Genome Wide Association Studies examined genetic factors predisposing individuals to schizophrenia and affective disorders (van der Hoorn et al., 2010). The paternal haplotype of the leucine rich repeat transmembrane neuronal 1 (LRRTM1) gene on chromosome-2p12, which is associated with left-handedness, was over-transmitted in individuals with schizophrenia and schizoaffective disorders (Francks et al., 2007). Other linkage studies of schizophrenia and lessened cerebral lateralization in adults implicate loci at chromosomes 17p11 (Francks et al., 2007), 10q28 (Van Agtmael, Forrest, & Williamson, 2002) and 12q21-23 (Warren, Stern, Duggirala, Dyer, & Almasy, 2006). Conversely, an epidemiological family study of handedness in 2,632 families, with 8,605 offspring, suggested an X chromosome transmission. Father's left-handedness was associated with greater influence in daughters' left-handedness. Mother's left-handedness yielded more left-handed sons (McKeever, 2000). Chromosome replications and epigenetic influences such as methylation or silencing of genes may also be factors associated with mental disorders and handedness (Klar, 2004).

The association between handedness and severity of psychiatric disorders in children has not been widely studied in the USA. The current study examined the prevalence of psychiatric co-morbidity and other indices of clinical severity of children with left-hand dominance compared to their right-handed peers in this clinical sample. It was hypothesized that children with left-handedness would have a more severe profile of psychiatric disorders.

METHODS

Participants

A case cohort design was used to compare psychiatric diagnoses and illness severity status of right-handed children with left-handed children treated at an

urban-based mental health centre. The first author evaluated and treated 718 children for mental health disorders and documented handedness on 692 children (95%). A majority of children in the study were African American ($n = 614$; 88%), males ($n = 435$; 62.9%) and right-handed ($n = 566$; 82%; Table 1). Other children were: White—74, Hispanic Mexican—1, Native American—1 and Native Canadian—2 (total other—11%). This study was approved by the Johns Hopkins Medical Institutions—Institutional Review Board.

Child's writing hand preference following a name writing request defined the child's handedness for this study. A study by Corey, Hurley, and Foundas (2001) used writing hand identification to compare left versus right hemisphere dominance. Writing hand correlated significantly with scores on handedness determination measures (Corey et al., 2001).

TABLE 1
Characteristics of study population by handedness ($N = 692$)

	<i>Total (N = 692)</i>		<i>Left-handed (n = 126)</i>		<i>Right-handed (n = 566)</i>		<i>p</i>
	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	
Male	435	62.9	81	64.3	354	62.5	.71
African American	614	88.7	113	89.7	501	88.5	.71
Psychiatric disorders							
Adjustment disorder	168	24.3	29	23.0	139	24.6	.72
ADHD	561	81.1	106	84.1	455	80.4	.33
Anxiety	446	64.5	93	73.8	353	62.4	.02
Depression	358	51.7	76	60.3	282	49.8	.03
Disruptive behaviour disorders	289	41.8	57	45.2	232	41.0	.38
Mood disorders	371	53.6	77	61.1	294	51.9	.06
Oppositional defiant disorder	277	40.0	65	51.6	212	37.5	.003
Psychosis	47	6.8	11	8.7	36	6.4	.34
Intellectual disability (IQ < 70)	56	8.1	10	7.9	46	8.1	.94
Pervasive developmental disorder	55	7.9	15	11.9	40	7.1	.07
Medications							
None	103	14.9	15	11.9	88	15.6	.30
Antidepressant	255	36.9	42	33.3	213	37.6	.37
Antipsychotics	191	27.6	44	34.9	147	26.0	.04
Anxiolytics	120	17.3	32	25.4	88	15.6	.008
Atomoxetine	55	8.0	11	8.7	44	7.8	.72
Mood stabilizer	129	18.6	26	20.6	103	18.2	.52
Stimulants	473	68.4	92	73.2	381	67.3	.23
Hospitalizations	155	22.4	38	30.1	117	20.7	.021
Residential	42	6.1	9	7.1	33	5.8	.58
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
Age (years)	10.1	3.2	9.6	3.4	10.2	3.1	.09
Psychiatric diagnoses	3.8	1.5	4.3	1.6	3.8	1.4	<.001

Data extraction

Demographic information (e.g., gender, age, race and ethnicity) was recorded prospectively; data were collected over a 12-year period ending in 2011. Data on diagnosis, medications used and hospitalizations were recorded. Diagnoses were based on *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) criteria (American Psychiatric Association, 2000). Medication categories were as follows: stimulants, including methylphenidate and dextroamphetamine preparations; antidepressants, including selective serotonin reuptake inhibitors and tricyclic antidepressants; functional anxiolytics, including guanfacine, clonidine, buspirone, hydroxyzine and benzodiazepines; mood stabilizing agents, including lithium, valproic acid and carbamazepine; first- and second-generation antipsychotics; and other, including atomoxetine. Hospitalizations were one or more inpatient mental health hospitalizations or “partial hospitalization” day hospital treatments. Residential treatments consisted of physician-supervised long-term psychiatric residential centres beyond short-term hospitalizations.

Severity of psychiatric disorders was defined by (1) the number of psychiatric diagnoses, (2) the number of different medication classes (e.g., stimulants, anxiolytics and antipsychotics) used and (3) the number of psychiatric hospitalizations. In studies of mental health services, researchers use psychiatric hospitalizations as an indicator of severity of psychiatric illness (Burns, 2007).

Statistical analysis

Descriptive statistics were used to summarize the characteristics of the cohort. *T*-test analyses compared means of continuous variables between right- and left-hand dominant children. Chi-squared analyses estimated whether the observed frequency distributions of psychiatric disorders and medication use by handedness differed from the theoretical distribution. Logistic regression models were developed to estimate the odds of psychiatric disorders and hospitalizations by handedness (referent was left-handed). Regression models were adjusted for demographic variables including age, gender and race (African American was referent). Statistical significance was set at a *p*-value of .05.

RESULTS

The rate of left-handedness in the study population was 18%. Comparing the proportion of left-hand dominance in the study population to that in the US population (estimated at 11.1%) yielded a statistically significant higher frequency of left-handedness in the clinical population, $p < .001$. Left-hand dominance did not differ by race or gender.

Number of psychiatric diagnoses

In the study cohort, the number of psychiatric diagnoses was significantly higher in children with left-handedness compared to their right-handed peers (mean 4.3 for left-handed children versus 3.8 for right-handed children, $p < .001$). In addition, children with left-handedness had significantly higher percentages of anxiety (73.8% in left-handed children versus 62.4% in right-handed, $p = .02$), depression (60.3% versus 49.8%, $p = .03$), mood disorder (61.1% versus 51.9%, $p = .06$) and oppositional defiant disorder (51.6% versus 37.5%, $p = .003$) compared to children who were right-handed (Table 1). The lowest rates of left-handedness compared to right-handedness were observed in adjustment disorders Not Otherwise Specified (NOS) (23.0% in left-handed children versus 24.6% right-handed children) and intellectual disability (IQ < 70; 7.9% versus 8.1%). Children with left-handedness had 31% higher odds of having a psychiatric diagnosis compared to their right-handed peers. Both unadjusted and adjusted odds of anxiety disorders, depressive disorders NOS and oppositional defiant disorder were significantly elevated for children who were left-handed (Table 2). Specifically, adjusted odds of psychiatric diagnoses were higher for left-handed children compared to right-handed children, ranging from 77% (95% CI: 1.17–2.68, $p = .007$) for depression to 64% (95% CI: 1.06–2.55, $p = .026$) for anxiety.

Other severity indices

Children with left-handedness also had a higher prevalence of psychiatric hospitalizations (30.1% for left-handed children versus 20.7% for right-handed children, $p = .021$). Children who were left-handed had 70% higher odds of psychiatric hospitalizations (95% CI: 1.10–2.63) following adjustment for demographic variables. Children who were left-handed were prescribed more

TABLE 2
Unadjusted and adjusted ORs of psychiatric disorders and psychiatric hospitalization for children with left-hand dominance ($N = 692$)

<i>Characteristics</i>	<i>Unadjusted OR</i>	<i>95% CI</i>	<i>Adjusted OR</i>	<i>95% CI</i>
Psychiatric diagnoses	1.31	1.15–1.50	1.31	1.15–1.50
Adjustment disorder	.91	.58–1.45	.98	.61–1.56
ADHD	1.29	.77–2.18	1.12	.63–1.97
Anxiety	1.70	1.10–2.62	1.64	1.06–2.55
Depression	1.53	1.03–2.27	1.77	1.17–2.68
Disruptive behaviour disorders	1.19	.81–1.75	1.19	.80–1.76
Mood disorders	1.45	.98–2.16	1.50	1.01–2.25
Oppositional defiant disorder	1.78	1.21–2.62	1.75	1.18–2.59
Psychosis	1.41	.70–2.85	1.47	.72–3.00
Psychiatric hospitalization	1.66	1.08–2.55	1.70	1.10–2.63

Adjusted for gender, age and race (referent: African American).

antipsychotic medications (34.9% for children with left-handedness versus 26.0% for children with right-handedness, $p = .04$) and anxiolytics (25.4% for children with left-handedness versus 15.6% for children with right-handedness, $p = .008$) than their right-handed peers.

DISCUSSION

The current study found a higher rate of left-handedness in this clinical sample of children receiving psychiatric care. Children in the cohort who were left-handed had greater clinical severity than their right-handed peers, measured by an increased number of psychiatric disorders, higher odds of hospitalization for treatment of psychiatric disorders and higher odds of being prescribed antipsychotic and anxiolytic drugs. Noteworthy, also, is the high rate of oppositional defiant disorder in left-handed children in this population compared to their right-handed peers. Thus, left-handedness may be a phenotypic marker for increased mental health severity and co-morbidity.

Genes and environmental factors influence the occurrence of both left-handedness and mental health disorders. Genes implicated in anxiety and depression include the following: CRHR1, the Corticotropin Releasing Hormone Receptor-1, 5-HTTLPR, the 5-HydroxyTryptamine (serotonin) Transporter Gene-Linked Polymorphic Region gene, and BDNF, the brain-derived neurotropic factor gene, among others (Boulle et al., 2012; Rogers et al., 2013; Webb et al., 2012). Environmental factors, such as maltreatment and violence exposure, also place individuals at higher risk for the development of depression, anxiety and post-traumatic stress (Anda et al., 2007; Rogers et al., 2013). Similarly, studies support the contribution of genetics to the expression of hand dominance (Francks et al., 2007; McKeever, 2000; Van Agtmael et al., 2002). Environmental factors such as variations in culture practice may also influence the prevalence and expression of left-handedness (Ida, Dutta, & Mandal, 2001). Prevalence of left-handedness varies across the world, with the highest rates in Europe (Great Britain and Russia, 9–12%; Kalichman, Korostishevsky, & Kobylansky, 2008; Leask & Crow, 2005) and lowest in Asia (Japan 3–5%; Ida et al., 2001). Left-handedness is reported in 5% of the children in Western Uganda, much lower than in the predominantly African American population in the current study (Holder & Kateeba, 2004).

Left-handedness may be a phenotypic marker associated with increased environmental vulnerabilities yielding higher prevalence of anxiety and depression. Arousal symptoms associated with post-traumatic stress disorder, an environmentally associated psychiatric disorder, are more severe in veterans who were left-handed (Choudhary & O'Carroll, 2007). Children with a history of prematurity and left- and mixed-hand preferences have lower performance on cognitive tests and are more likely to meet DSM criteria for attention deficit

hyperactivity disorder (ADHD; Ross, Lipper, & Auld, 1992). Children in this study's clinical cohort may have significant exposure to urban environmental risks such as poverty and violence exposure that may be associated with an increased severity of psychiatric disorders.

One potential limitation of this study is the method used for assessing handedness. Non-right-handedness is frequently evaluated by several motor functional measures that include, but are not restricted to, identifying the writing hand (Corey et al., 2001). However, in the clinical setting, the writing hand is a measure easily obtained. Another limitation of the study is that the majority of subjects were African American, which may limit the generalizability of the findings. Importantly, African American children are frequently underserved in the mental health system; thus, this study is innovative and important because few studies document the association a phenotypic finding such as left-handedness and psychiatric illness in a population of African American children (US Surgeon General releases report on mental health: culture, race, and ethnicity, 2001). Finally, there may be incomplete clinical data, a weakness that is offset by the inclusion of 95% of subjects evaluated by the first author.

This is one of the first studies of the association between handedness and mental health disorders in a predominantly African American urban population. We consider this is a critical first step in identifying phenotypic risk factors, possibly associated with environmental and genetic vulnerability to psychiatric disorders. Future studies should include children from other racial and ethnic populations. Delineating genotypes underlying the association between left-handedness and severity of psychiatric illness would also be a logical next step. Recognition of the increased risk associated with left-handedness may result in increased clinical vigilance and early identification of mental health needs, especially in the African American urban population.

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