Hirnstein & Hugdahl Excess of non-right-handedness in schizophrenia

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ONLINE SUPPLEMENT

Non-right-handedness subdivided in left- and mixed-handedness

Non-right-handedness comprises both left- and mixed-handers. Since there have been claims that schizophrenia is characterised by a lack of lateralisation, it has been hypothesised that the excess of non-right-handedness in schizophrenia is mostly the consequence of an excess of mixed-handers.^{1–3} We therefore carried out three additional meta-analyses. The first explored whether there is an excess of left- compared with right-handers in schizophrenia. To this end, only studies were included with a dichotomous handedness definition. That is, individuals were either classified as left- or right-handers. In a second meta-analysis we examined whether there is an excess of mixed-handers compared with lateralised individuals (i.e. individuals *without* a strong hand preference *v*. individuals *with* a strong hand preference irrespective of preference direction). Here, only studies were included that used either a dichotomous mixed- *v*. lateralised or a trichotomous left-/mixed-/right-hander definition, whereby left- and right-handers were collapsed. The studies with a trichotomous classification further allowed comparing strong left- to strong right-handers by excluding the mixed-handers. The search criteria and statistical procedures were identical to the main non-right-handedness meta-analysis.

Results

Left- v. right-handers

The meta-analysis that controlled for gender comprised three effect sizes for females (patients: n=661, controls: n=1243) and seven for males (patients: n=2210, controls: n=52208). For a comprehensive list of the included studies see Table DS1. Male patients with schizophrenia were

significantly more often left-handed than male controls (odds ratio (OR)=1.81, 95% CI 1.16–2.82, Z=2.62, P=0.009). In females, a trend for the same pattern emerged (OR=1.94, 95% CI 0.94–4.02, Z=1.78, P=0.074). There was no significant difference between females and males (Q(1)=0.03, P=0.873) but the overall OR=1.85 (95% CI 1.26–2.70, I^2 =5.44, Q(9)=9.52) was significant (Z=3.17, P=0.002).

The meta-analysis that controlled for handedness assessment comprised data from 1702 patients and 4682 controls (6 effect sizes) that had been tested behaviourally. 2527 patients and 51881 controls (24 effect sizes) had been studied with other forms of assessment. Both behavioural (OR=1.95, 95% Cl 1.54–2.47, *Z*=5.57, *P*<0.001) and other forms of handedness assessment (OR=1.50, 95% Cl 1.24–1.83, *Z*=4.10, *P*<0.001) showed that left-handedness is more prevalent in schizophrenia than in controls. There was a trend towards stronger left-handedness in schizophrenia when handedness was assessed behaviourally (*Q*(1)=2.78, *P*=0.095). The overall OR=1.67 (95% Cl 1.44–1.95, l^2 =1.37, *Q*(29)=29.40) was significant (*Z*=6.71, *P*<0.001). The results for the meta-analyses that controlled for gender and behavioural assessment of handedness are shown in Fig. DS2 A and B respectively. There were only four effect sizes available where handedness was assessed behaviourally *and* information on the participants' gender was provided (1 OR for females, 3 OR for males). Therefore, no meta-analysis that combined the two effects was performed.

Mixed-handers v. lateralised individuals

There were 7 effect sizes for females (patients: n=168, controls: n=666) and 10 effect sizes for males (patients: n=630, controls: n=1728) available. For a comprehensive list of the included studies see Table DS2. The overall OR=1.71 (95% CI 1.16–2.52, $l^2=15.79$, Q(16)=19.00) differed significantly from 1 (Z=2.69, P=0.007), indicating patients have 1.7 times the odds of being mixed-handed compared with controls (Fig. DS3A). Females showed a significant OR=2.64 (95% CI 1.24–5.62, Z=2.52, P=0.012), whereas males did not (OR=1.46, 95% CI 0.93-2.19, Z=1.63, P=0.103). However, there was no significant gender effect (Q=1.75, P=0.186). Likewise, the odds of being mixed-handed were elevated in schizophrenia when compared with controls for both behavioural (OR=2.13, 95% CI 1.12–4.03, *Z*=2.32, *P*=0.020) and other forms of handedness assessments (OR=1.71, 95% CI 1.23–2.38, *Z*=3.19, *P*=0.001). This was based on 5 effect sizes for behavioural (patients: *n*=436, controls: *n*=329) and 25 effect sizes (patients: *n*=1935, controls: *n*=5857) for other forms of handedness assessment (Fig. DS3B). As a result the overall effect was also significant (OR=1.79, 95% CI 1.34–2.41, l^2 <0.01, *Q*(29)=27.09, *Z*=3.90, *P*<0.001). The difference between the methods, however, was not (*Q*(1)=0.35, *P*=0.555). Again, no combined meta-analysis that controlled for gender and handedness assessment was carried out, because there were only 3 effect sizes available, 1 OR for females and 2 for males.

Strong left- v. strong right-handers

Four of the studies used in the mixed-handers versus lateralised comparison had to be excluded because they did not differentiate between strong left- and right-handers.^{2,4–6} All other studies from Table DS2 were included. Since there were no strong left-handers in the sample of Gureje,⁷ 0.5 was added to each cell to be able to compute OR (else: division by zero).

There were 6 effect sizes for females (patients: n=122, controls n=566) and 7 effect sizes for males (patients n=236, controls n=524). The overall OR=1.38 (95% CI 0.80–2.38, l^2 <0.01, Q(12)=9.88) was not significant 1 (Z=1.16, P=0.247), neither was the OR for females (OR=0.80, 95% CI 0.31–2.07, Z=0.46, P=0.645). Males showed a trend (OR=1.80, 95% CI 0.93–3.49, Z=1.74, P=0.083), but the difference between males and females did not reach significance (Q(1)=1.88, P=0.171). For results see Fig. DS4A.

The meta-analysis that controlled for handedness assessment did not reveal any significant deviations from 1 (Fig. DS4B), neither for behavioural studies (OR=0.50, 95% CI 0.16–1.55, *Z*=1.20, *P*=0.230) nor other forms of handedness assessment (OR=1.24, 95% CI 0.94–1.64, *Z*=1.54, *P*=0.124) nor the overall effect (OR=1.18, 95% CI 0.90–1.55, I^2 =4.97, Q(25)=26.31, *Z*=1.21, *P*=0.225). There was also no significant difference between behavioural and other forms of assessment (Q(1)=2.34, *P*=0.126). This was based on 4 effect sizes for behavioural (patients: *n*=190, controls: *n*=189) and 22

effect sizes for other forms of handedness assessment (patients: *n*=1470, controls: *n*=4301). There was only one study that assessed handedness behaviourally and provided information on the participants' gender. Therefore, no meta-analysis was carried out that combined the two effects.

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Study	Diagnosis	Handedness	Schizo	phrenia	Сог	ntrol
		determination	n = nonright	n = right	n = nonright	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Wahl 1976 (8) ^ª	Not specified	10 questions about manual activities (four participants additionally performed the items)	2 (n/a)	19 (n/a)	1 (n/a)	17 (n/a)
Chaugule & Master 1981 (9)	ICD-8	Behavioral (demonstration of Annett's questionnaire)	63 (42, 21)	30 (18, 12)	76 (50, 26)	74 (48, 26)
Taylor et al. 1982 ^b (10)	British Glossary to the 8th Edition of the International Classification of Diseases (1968).	Annett's questionnaire	12 (10, 2)	90 (41, 49)	107 (48, 59)	693 (309, 384)
Kameyama et al. 1983 (11)	Research Diagnostic Criteria	Other questionnaire	86 (n/a)	498 (n/a)	121 (n/a)	565 (n/a)
Manschreck & Ames 1984 (12)	DSM-III	Behavioral (based on writing, kicking a ball and looking out of a paper tube)	27 (n/a)	26 (n/a)	16 (n/a)	4 (n/a)
Merrin 1984 (13)	Research Diagnostic Criteria	Other questionnaire	9 (9, 0)	43 (43, 0)	11 (11, 0)	38 (38, 0)
Yan et al. 1985 (14)	Feighner (1972) Criteria	Behavioral (demonstration of manual actions)	45 (21, 24)	180 (106, 74)	30 (17, 13)	402 (183, 219)

Study	Diagnosis	Handedness	Schizo	phrenia	Cor	ntrol
		determination	n = nonright	n = right	n = nonright	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Hauser et al. 1988 (15)	Research Diagnostic Criteria	Behavioral (ten item performance laterality scale from Schroeder Block Campbell Psychiatric Sensory Integration Evaluation 1978)	25 (15, 10)	40 (31, 9)	15 (13, 2)	50 (33, 17)
Green et al. 1989 (16)	DSM-III	Behavioral (demonstration of manual actions)	38 (n/a)	55 (n/a)	19 (n/a)	86 (n/a)
Breier et al. 1992 (17)	DSM-III-R	not specified	9 (n/a)	35 (n/a)	5 (n/a)	24 (n/a)
Chengappa et al. 1992 (18)	Research Diagnostic Criteria	Presumably behavioral (based on writing, kicking a ball and looking out of a paper tube, c.f. Manschreck & Ames, 1984)	40 (24, 16)	146 (75, 71)	75 (34, 41)	271□ (102, 169)
Cannon et al. 1995 (19)	DSM-III	Behavioral (demonstration of EHI items)	37 (30, 7)	56 (37, 19)	8 (5, 3)	35 (16, 19)
Corey-Bloom et al. 1995 (20)	DSM-III-R	not specified	2 (n/a)	28 (n/a)	3 (n/a)	25 (n/a)
Green & Rieg 1995 (21)	DSM-III-R	Self-report of writing hand	27 (n/a)	59 (n/a)	64 (n/a)	312 (n/a)

Study	Diagnosis	Handedness	Schizo	phrenia	Cor	itrol
		determination	n = nonright	n = right	n = nonright	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Crow et al. 1996 (1) ^c	Syndrome Check	mothers of participants	11 (n/a)	20 (n/a)	243 (n/a)	1241 (n/a)
	List of the Present	reported handedness				
	State Examination	narrow definition of				
	(Wing et al., 1974)	Annett classification is				
	and the Catego	used				
	System					
Fukuzako et al. 1996 (22)	DSM-III-R	EHI	2 (n/a)	29 (n/a)	1 (n/a)	30 (n/a)
Malesu et al. 1996 (23)	Research	Annett's questionnaire	42 (n/a)	78 (n/a)	29 (n/a)	57 (n/a)
Cannon et al. $1007(24)$		Rehavioral (hand used for	1 (3 1)	20 (15 5)	380 (223-166)	3564 (1882
	DOM III K	writing and drawing was	+ (0, 1)	20 (10, 0)	303 (223, 100)	1682)
		observed and recorded)				1002)
Hinsberger et al. 1997	DSM-III-R	not specified	1 (n/a)	9 (n/a)	2 (n/a)	8 (n/a)
(25)						
Cannon et al. 1998 (26)	DSM-III-R	not specified	6 (n/a)	69 (n/a)	9 (n/a)	107 (n/a)
Sperling et al. 1999 (27)	ICD-10	Other questionnaire	19 (14, 5)	41 (16, 25)	5 (3, 2)	55 (27, 28)
Bilder et al. 2000 (28)	Research	EHI	27 (n/a)	67 (n/a)	9 (n/a)	27 (n/a)
	Diagnostic Criteria					
Löw et al. 2000 (29)	DSM-IV	EHI	2 (n/a)	10 (n/a)	1 (n/a)	11 (n/a)
Baaré et al. 2001 (30)	DSM-IV	probably based on 10	4 (n/a)	25 (n/a)	17 (n/a)	70 (n/a)
		items in the CASH				
		interview				
Egan et al. 2001 (31)	DSM-IV	EHI	50 (n/a)	65 (n/a)	86 (n/a)	187 (n/a)
Hulshoff Pol et al. 2001 ^d	DSM-IV	CASH interview	23 (n/a)	136 (n/a)	26 (n/a)	132 (n/a)
(48)						
Matsumoto et al. 2001 (32)	DSM-IV	Annett's questionnaire	8 (n/a)	32 (n/a)	9 (n/a)	31 (n/a)
Reilly et al. 2001 (33)	DSM-III	EHI	12 (6, 6)	18 (13, 5)	9 (4, 5)	28 (14, 14)

Study	Diagnosis	Handedness	Schizo	phrenia	Cor	ntrol
		determination	n = nonright	n = right	n = nonright	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Job et al. 2002 (34)	not specified,	writing hand, not further	3 (n/a)	31 (n/a)	5 (n/a)	31 (n/a)
	referred to APA	specified				
Kemether et al. 2003 (35)	DSM-IV	EHI	5 (n/a)	36 (n/a)	2 (n/a)	58 (n/a)
Umbricht et al. 2003 (36)	DSM-IV	Chapman & Chapman scale (1987)	4 (n/a)	22 (n/a)	3 (n/a)	22 (n/a)
Buchanan et al. 2004 (37)	DSM-III-R & IV	not specified	3 (n/a)	41 (n/a)	1 (n/a)	33 (n/a)
Byrne et al. 2004 ^e (38)	DSM-IV	Behavioral (demonstration of EHI & Annette's questionnaire)	4 (n/a)	13 (n/a)	6 (n/a)	23 (n/a)
Szeszko et al. 2004 (39)	DSM-IV	modified EHI	1 (n/a)	13 (n/a)	3 (n/a)	13 (n/a)
Upadhyay et al. 2004 ^t (40)	DSM-IV	Waterloo Handedness Questionnaire	7 (n/a)	30 (n/a)	18 (n/a)	182 (n/a)
Bonner-Jackson et al. 2005 (41)	DSM-IV	EHI	3 (n/a)	14 (n/a)	3 (n/a)	23 (n/a)
Moreno et al. 2005 (42)	DSM-IV	not specified	2 (n/a)	21 (n/a)	6 (n/a)	31 (n/a)
Ortuno et al. 2005 (43)	DSM-IV	Annett's questionnaire	29 (16, 13)	33 (21, 12)	59 (35, 24)	87 (38, 49)
Tamagaki et al. 2005 (44)	DSM-III-R & IV	Not specified	7 (4, 3)	51 (32, 19)	8 (3, 5)	48 (31, 17)
Greenstein et al. 2006 (45)	DSM-IV	not specified	15 (n/a)	51 (n/a)	8 (n/a)	64 (n/a)
Barch & Csernansky 2007 (46)	DSM-IV	EHI	8 (n/a)	49 (n/a)	14 (n/a)	106 (n/a)
Glenthoj et al. 2007 (47)	ICD-10	not specified	6 (n/a)	13 (n/a)	2 (n/a)	17 (n/a)
Narr et al. 2007 (48)	DSM-IV	Behavioral (demonstration of modified EHI)	16 (12, 4)	68 (48, 20)	10 (7, 3)	57 (23, 34)
Dane et al, 2009 (49)	DSM-IV	EHI	33 (27, 6)	55 (33, 22)	29 (17, 12)	89 (43, 46)

Study	Diagnosis	Handedness	Schizo	phrenia	Cor	ntrol
		determination	n = nonright	n = right	n = nonright	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Potkin et al. 2009 (50)	DSM-IV	EHI	13 (n/a)	115 (n/a)	13 (n/a)	115 (n/a)
Bachmann et al. 2010 (51)	DSM-IV	EHI	7 (n/a)	8 (n/a)	1 (n/a)	17 (n/a)
Deep-Soboslay et al. 2010 ^g (52)	DSM-IV	Behavioral (demonstration of EHI)	80 (66, 14)	295 (225, 70)	188 (93, 95)	882 (372, 510)
Witthaus et al. 2010 (53)	DSM-IV	EHI	10 (n/a)	13 (n/a)	6 (n/a)	23 (n/a)
Lewine (personal communication) ^h	DSM-III-R	Raczkowski et al. (1974) and Annett's questionnaire	90 (67, 23)	101 (59, 42)	35 (16, 19)	60 (24, 36)
Takahashi (personal communication) ⁱ	DSM-III-R	EHI	8 (6, 2)	38 (28, 10)	3 (3, 0)	57 (35, 22)

EHI = Edinburgh Handedness Inventory. If Annett's questionnaire (54) was used, the narrow criteria were applied except (43). ^a if participants with inconstant handedness reports are removed; ^b reclassification of Fleminger et al. (1977) with only schizophrenic patients; ^c "narrow" schizophrenia criteria were used; ^d "left" and "right" in Table 1 is flipped; ^e criterion for nonright-handedness was LQ < 80; ^f based on "% left", "% mixed" and "% right" in Table 2; ^g the number of male and female participants are based on personal communication; ^h partly reported in (55, 56); ⁱ partly reported in (57, 58)

Study	Diagnosis	Handedness determination	Schizo	phrenia	Сог	ntrol
			n = left	n = right	n = left	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Dvirskii 1976 (59)	"classification of the Institute of Psychiatry, Academy of Medical Sciences of the USSR"	Behavioral (manual actions were observed)	93 (61, 32)	1177 (599, 578)	176 (111, 65)	4164 (2079, 2085)
Gur 1977 (60)	"mental status examination, previous history, and an evaluation of the patient's behavior on the ward"	Other questionnaire	32 (n/a)	168 (n/a)	22 (n/a)	178⊡ (n/a)
Tolor 1981 ^a (61)	"diagnosis was established by hospital staff"	Behavioral (hand that was used to complete informed consent was observed)	8 (n/a)	82 (n/a)	6 (n/a)	44 (n/a)
Nasrallah et al. 1982 (62)	DSM-III	Behavioral ("A13-item performance laterality scale for eye, hand, and foot dominance" was used)	15 (15, 0)	65 (65, 0)	5 (5, 0)	78□ (78,0)
Piran et al. 1982 (63)	DSM-III	Behavioral (demonstration with objects)	6 (n/a)	20 (n/a)	2 (n/a)	14⊡ (n/a)
De Lisi et al. 1991 (64)	DSM-III-R	not specified	7 (n/a)	34 (n/a)	2 (n/a)	18 (n/a)

 Table DS2 List of studies included in the meta-analysis on left- versus right-handers (supplemental material)

Study	Diagnosis	Handedness determination	Schizo	phrenia	Cor	ntrol
			n = left	n = right	n = left	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Harvey et al. 1993 (65)	Research Diagnostic Criteria	Annett's questionnaire	5 (n/a)	43 (n/a)	4 (n/a)	30 (n/a)
Clementz et al. 1994 (66)	DSM-III	EHI	11 (n/a)	47 (n/a)	12 (n/a)	107 (n/a)
David et al. 1995 (67)	ICD 8/DSM-III-R	Oral self-report	19 (19, 0)	177 (177, 0)	4160 (4160, 0)	45551 (45551, 0)
Flaum et al. 1995 (68)	DSM-III-R	not specified	8 (4, 4)	94 (66, 28)	7 (4, 3)	80 (41, 39)
O'Callaghan et al. 1995 (69)	DSM-III	EHI	9 (n/a)	36 (n/a)	5 (n/a)	19 (n/a)
Taylor & Amir 1995 (6)	DSM-III	Behavioral (demonstration of EHI items)	23 (23, 0)	140 (140, 0)	5 (5, 0)	107 (107, 0)
Frangou et al. 1997 (70)	DSM-III-R	Annett's questionnaire	3 (n/a)	29 (n/a)	8 (n/a)	86 (n/a)
Russell et al. 1997 (71)	DSM-III-R	not specified	4 (n/a)	18 (n/a)	0	22□ (n/a)
Sowell et al. 2000 (72)	DSM-III-R	not specified	0	9 (n/a)	1 (n/a)	9□ (n/a)
Narr et al. 2001 (73)	DSM-III-R	Annett's questionnaire	2 (n/a)	23 (n/a)	2 (n/a)	26⊡ (n/a)
Buijsrogge et al. 2002 ^c (74)	DSM-IV	Behavioral (demonstration of EHI items)	6 (n/a)	67 (n/a)	1 (1, 0)	80□ (51, 29)
Csernansky et al. 2002 (75)	DSM-IV	EHI	6 (n/a)	46 (n/a)	3 (n/a)	62□ (n/a)
Panizzon et al. 2003 (76)	DSM-III-R	Presumably self-report of writing hand	13 (10, 3)	58 (42, 16)	0	67 (49, 18)
Seidman et al. 2003 (77)	DSM-III-R	Annett's questionnaire	11 (n/a)	68 (n/a)	8 (n/a)	76 (n/a)
Liu et al. 2004 (78)	DSM-IV	EHI	1 (n/a)	72 (n/a)	2 (n/a)	69 (n/a)
Upadhyay et al. 2004 ^d (40)	DSM-IV	Waterloo Handedness Questionnaire	3 (n/a)	34 (n/a)	10 (n/a)	190 (n/a)

Table DS2 List of studies included in the meta-analysis on left- versus right-handers (supplemental material) (continued)

Study	Diagnosis	Handedness determination	Schizo	phrenia	Cor	ntrol
			n = left	n = right	n = left	n = right
			(males, females)	(males, females)	(males, females)	(males, females)
Kasparek et al. 2007 (79)	ICD-10	not specified	3 (3, 0)	19 (19, 0)	3 (3, 0)	15 (15, 0)
Whitford et al. 2007 (80)	DSM-IV	not specified	7 (n/a)	34 (n/a)	8 (n/a)	39 (n/a)
Meisenzahl et al. 2010 (81)	DSM-IV	EHI	4 (n/a)	85 (n/a)	9 (n/a)	129 (n/a)
Rametti et al. 2010 (82)	DSM-IV	not specified	1 (n/a)	22 (n/a)	0	23 (n/a)
Nishimura et al. 2011 (83)	DSM-IV	EHI	2 (n/a)	12 (n/a)	2 (n/a)	38 (n/a)
Cobia et al.2012 (84)	DSM-IV	not specified	2 (n/a)	18 (n/a)	4 (n/a)	16 (n/a)
Da Silva et al. 2012 (85)	multicenter-study,	Self-report of writing-				
	at least partly based on DSM-IV	hand	141 (n/a)	1028 (n/a)	46 (n/a)	643 (n/a)
Ettinger et al. 2012 (86)	DSM-IV	Annett's questionnaire	11 (n/a)	48 (n/a)	7 (n/a)	63 (n/a)

Table DS2 List of studies included in the meta-analysis on left- versus right-handers (supplemental material) (continued)

EHI = Edinburgh Handedness Inventory. If Annett's questionnaire (54) was used, the narrow criteria were applied.^a general population was taken as control

sample; ^b "left" and "right" in Table 1 is flipped; ^c when handedness is based on writing; ^d when handedness is based on writing as in Dragovic & Hammond

(87)

Table DS3 List of studies included in the meta-analyses on mixed-handers versus lateralized individuals and strong left- versus strong right-handers

(supplemental material)

Study	Diagnosis	Handedness determination	Schizophrenia	Control
			n = right/left/mixed (males, females)	n = right/left/mixed (males, females)
Wahl 1976 ^a (8)	Not specified	10 questions about manual activities (four participants additionally performed the items)	19/1/1 (n/a)	17/0/1 (n/a)
Taylor et al. 1982 ^b (10)	British Glossary to the 8th Edition of the International Classification of Diseases (1968).	Annett's questionnaire	90/8/4 (41/6/4, 49/2/0)	693/40/67 (309/18/30, 384/22/37)
Kameyama et al. 1983 (11)	Research Diagnostic Criteria	Other questionnaire	498/30/56 (n/a)	565/33/88 (n/a)
Merrin 1984 (13)	Research Diagnostic Criteria	Other questionnaire	43/4/5 (43/4/5, 0/0/0)	38/1/10 (38/1/10, 0/0/0)
Gureje 1988 (7)	St Louis criteria	Behavioral (demonstration of manual actions)	62/0/8 (n/a)	32/0/8 (n/a)
Green et al. 1989 (16)	DSM-III	Behavioral (demonstration of manual actions)	55/2/36 (n/a)	86/4/15 (n/a)
Green & Rieg 1995 (21)	DSM-III-R	Self-report of writing hand	59/17/10 (n/a)	312/48/16 (n/a)
Cannon et al. 1995 (19)	DSM-III	Behavioral (demonstration	56/2/35	35/3/5
		of EHI items)	(37/1/29, 19/1/6)	(16/1/4, 19/2/1)
Taylor & Amir 1995 ^c (6)	DSM-III	Behavioral (demonstration	*42/121	*17/95
		of EHI items)	(42/121, 0/0)	(17/95, 0/0)

Table DS3 List of studies included in the meta-analysis on mixed-handers versus lateralized individuals and strong left- versus strong right-handers (supplemental material) (continued)

Study	Diagnosis	Handedness determination	Schizophrenia	Control
			n = right/left/mixed	n = right/left/mixed
			(males, females)	(males, females)
Malesu et al. 1996 (23)	Research Diagnostic Criteria	Annett's questionnaire	78/6/36 (n/a)	57/8/21 (n/a)
Crow et al. 1996 (1) ^d	Syndrome Check List of the Present State Examination	mothers of participants reported handedness parrow definition of Appett	20/3/8 (n/a)	1241/140/103 (n/a)
	(Wing et al., 1974) and the Catego System	classification is used		
Orr et al. 1999 (2)	DSM-III	Annett's questionnaire	*79/15	*82/3
l öw et al. 2000 (29)	DSM-IV	EHI	(70/9, 9/0) 12/0/2 (n/a)	(33/3, 29/0) 11/1/0 (n/a)
Baaré et al. 2001 (30)	DSM-IV	probably based on 10 items in the CASH interview	25/4/0 (n/a)	70/15/2 (n/a)
Egan et al. 2001 (31)	DSM-IV	EHI	65/8/42 (n/a)	187/5/81 (n/a)
Giotakos 2001 (5)	DSM-III-R	Annett's questionnaire	*58/10	*847/97
			(58/10, 0/0)	(847/97, 0/0)
Hulshoff Pol et al. 2001 ^e (88)	DSM-IV	CASH interview	136/20/3 (n/a)	132/23/3 (n/a)
Reilly et al. 2001 (33)	DSM-III	EHI	18/1/11	28/3/6
			(13/1/5, 5/0/6)	(14/1/3, 14/2/3)
Job et al. 2002 (34)	not specified, referred to APA	writing hand, not further specified	31/1/2 (n/a)	31/3/2 (n/a)
Kemether et al. 2003 (35)	DSM-IV	EHI	36/1/4 (n/a)	58/2/0 (n/a)

 Table DS3 List of studies included in the meta-analysis on mixed-handers versus lateralized individuals and strong left- versus strong right-handers (supplemental material) (continued)

Study	Diagnosis	Handedness	Schizophrenia	Control
		determination	n = right/left/mixed (males, females)	n = right/left/mixed (males, females)
Byrne et al. 2004 ^f (38)	DSM-IV	Behavioral (demonstration of EHI & Annette's questionnaire)	13/0/4 (n/a)	25/4/4 (n/a)
Collinson et al. 2004 ^g (4)	DSM-IV	Annett's questionnaire	*35/9 (n/a)	*34/5 (n/a)
Upadhyay et al. 2004 ^h (40)	DSM-IV	Waterloo Handedness Questionnaire	30/1/6 (n/a)	182/8/10 (n/a)
Moreno et al. 2005 (42)	DSM-IV	not specified	21/1/1 (n/a)	31/4/2 (n/a)
Ortuno et al. 2005 (43)	DSM-IV	Annett's questionnaire	33/3/26 (21/2/14, 22/0/12)	87/8/51 (38/4/31, 49/4/20)
Glenthoj et al. 2007 (47)	ICD-10	not specified	13/5/1 (n/a)	17/2/0 (n/a)
Dane et al. 2009 (49)	DSM-IV	EHI	55/0/33 (33/0/27, 22/0/6)	89/6/23 (43/4/13, 46/2/10)
Bachmann et al. 2010 (51)	DSM-IV	EHI	8/3/4 (n/a)	17/0/1 (n/a)
Witthaus et al. 2010 (53)	DSM-IV	EHI	13/5/5 (n/a)	23/5/1 (n/a)
Takahashi (personal	DSM-III-R	EHI	38/7/1	57/2/1
communication) ⁱ			(28/6/0, 10/1/1)	(35/2/1, 22/0/0)

EHI = Edinburgh Handedness Inventory. If Annett's questionnaire (54) was used, the narrow criteria were applied except (43). * left- and right-handers are collapsed to lateralized participants as no separate information on left- and right-handers is provided ^a if participants with inconstant handedness reports are removed; ^b reclassification of (89) with only schizophrenic patients; ^c based on "pure handedness" from Table 1 ^d "narrow" schizophrenia criteria were used; ^e "left" and "right" in Table 1 is flipped; ^f criterion for mixed was 80 < LQ > -80; ^g narrow definition of Annett classification is used and the control sample tested by the authors; ^h based on "% left", "% mixed" and "% right" in Table 2; ⁱ partly reported in (57, 58)

 Table DS4 Overview of electronic literature search

Platform	Used key words	Total no. of articles obtained
Pubmed	Handedness AND Schizophrenia	
(http://www.ncbi.nlm.nih.gov/pubmed)	AND Gender	102
	Handedness AND Schizophrenia	403
	AND Sex	
ISI Web of knowledge	Handedness AND Schizophrenia	
(http://www.webofknowledge.com/)	AND Gender	170
	Handedness AND Schizophrenia	175
	AND Sex	
PsycINFO		
(http://www.apa.org/pubs/databases/ps vcinfo/index_aspx)	Handedness AND Schizophrenia AND Sex	3

Note: There were no language restrictions.

Fig. DS1 Forest plot for non-right-handedness in studies that assessed handedness behaviourally or with other methods.

Study name	Odds ratio	Lower Limit	Upper Limit	р	Odds ratio and 95% CI
Behavioural assessment					
Chaugule & Master 1981 (42)	2.04	1.19	3.51	0.01	
Manschreck & Ames 1984 (58)	3.85	1.14	13.06	0.03	
Yan et al. 1985 (71)	3.35	2.04	5.49	< 0.01	
Hauser et al. 1988 (19)	2.08	0.97	4.47	0.06	
Green et al. 1989 (50)	3.13	1.64	5.97	< 0.01	
Chengappa et al. 1992 (43)	0.99	0.64	1.53	0.96	
Cannon et al. 1995 (4)	2.89	1.21	6.92	0.02	
Cannon et al. 1997 (40)	1.83	0.62	5.39	0.27	
Byrne et al. 2004 (27)	1.18	0.28	4.96	0.82	
Narr et al. 2007 (62)	1.34	0.56	3.19	0.51	
Deep-Soboslay et al. 2010 (16)	1.27	0.95	1.71	0.11	
Behavioural ass. overall	1.90	1.42	2.53	<0.01	
Other forms of assessment					
Wahl 1976 (7)	1.79	0.15	21.54	0.65	
Taylor et al. 1982 (67)	0.86	0.46	1.63	0.65	
Kameyama et al. 1983 (18)	0.81	0.60	1.09	0.16	· · · · · · ·
Merrin 1984 (60)	0.72	0.27	1.93	0.52	
Breier et al. 1992 (38)	1.23	0.37	4.14	0.73	
Corey-Bloom et al. 1995 (44)	0.60	0.09	3.86	0.59	
Green & Rieg 1995 (51)	2.23	1.31	3.79	< 0.01	
Crow et al. 1996 (45)	2.81	1.33	5.94	0.01	
Fukuzako et al. 1996 (48)	2.07	0.18	24.07	0.55	
Malesu et al. 1996 (57)	0.44	0.59	1.90	0.85	
Connon of al 1997 (31)	1.02	0.03	2.00	0.04	
Cannon et al. 1996 (41)	T.03	1.30	3.03	<0.95	
Bilder et al. 2000 (27)	5.10	0.50	2 01	<0.01	
Löw et al. 2000 (57)	2 20	0.30	2.91	0.54	
Baaré et al. 2000 (30)	0.66	0.17	20.14	0.04	
Egan et al. 2001 (47)	1.67	1.07	2.10	0.43	
Hulshoff Pol et al. 2001 (53)	0.86	0.47	1.58	0.62	
Matsumoto et al. 2001 (59)	0.86	0.29	2.52	0.78	
Reilly et al. 2001 (64)	2.07	0.73	5.91	0.17	
Job et al. 2002 (54)	0.60	0.13	2.73	0.51	
Kemether et al. 2003 (55)	4.03	0.74	21.87	0.11	
Umbricht et al. 2003 (68)	1.33	0.27	6.67	0.73	
Buchanan et al. 2004 (39)	2.41	0.24	24.30	0.45	
Szeszko et al. 2004 (65)	0.33	0.03	3.64	0.37	
Upadhyay et al. 2004 (69)	2.36	0.91	6.13	0.08	
Bonner-Jackson et al. 2005 (30)	1.64	0.29	9.29	0.57	
Moreno et al. 2005 (61)	0.49	0.09	2.68	0.41	
Ortuno et al. 2005 (22)	1.30	0.71	2.36	0.40	
Tamagaki et al. 2005 (66)	0.82	0.28	2.45	0.73	
Greenstein et al. 2006 (52)	2.35	0.93	5.99	0.07	
Barch & Csernansky 2007 (36)	1.24	0.49	3.14	0.66	
Glenthoj et al. 2007 (49)	3.92	0.68	22.70	0.13	
Dane et al. 2009 (46)	1.84	1.01	3.36	0.05	
Potkin et al. 2009 (63)	1.00	0.44	2.25	1.00	
Bachmann et al. 2010 (35)	14.87	1.56	142.20	0.02	
withous et al. 2010 (70)	2.95	0.87	9.98	0.08	
Takabashi (personal communication)	1.03	1.00	2.03	0.10	
Other forms of ass_overall	4.00	1.00	1 60	<0.05	
Cambined	1.09	1.15	1.09	-0.01	
Combined	1.53	1.31	1.80	<0.01	•
					0.01 0.1 1 10 100
					More non-right-handers More non-right-handers
					in control group in schizophrenia patients

Fig. DS2 Forest plot for left- versus right-handers in (A) females compared with males and (B) studies

that assessed handedness behaviourally compared to other forms of assessment.



Fig. DS3 Forest plot for mixed-handers- versus lateralized individuals in (A) females compared to

males and (B) studies that assessed handedness behaviourally compared with other forms of

assessment.



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Fig. DS4 Forest plot for strong left- versus strong right-handers in (A) females compared to males and

(B) studies that assessed handedness behaviourally compared with other forms of assessment.

Δ	Statistics for each study							
Study name	Odds ratio	Lower Limit	Upper Limit	р		Odds ratio	and 95% Cl	
Females Taylor et al. 1982 (10) Cannon et al. 1995 (19) Reilly et al. 2001 (33) Ortuno et al. 2005 (43) Dane et al. 2009 (49) Takahashi (personal communication) Females overall Males Taylor et al. 1982 (10) Merrin 1984 (13) Cannon et al. 1995 (19) Reilly et al. 2001 (33) Ortuno et al. 2005 (43) Dane et al. 2009 (49) Takahashi (personal communication) Males overall	0.71 0.50 0.53 1.02 0.41 6.43 0.80 2.51 3.53 0.43 1.08 0.90 0.14 3.75 1.80	0.16 0.04 0.02 0.24 0.31 0.94 0.38 0.03 0.06 0.15 0.01 0.70 0.93 0.80	3.12 5.99 12.82 9.98 8.97 171.42 2.07 6.69 33.02 7.35 19.05 5.36 2.77 20.03 3.49	0.65 0.58 0.69 0.99 0.57 0.27 0.65 0.07 0.27 0.56 0.96 0.91 0.20 0.12 0.02				•
Compined	1.38	0.80	2.38	0.25	0.0	1 0.1	1 10	100

More strong left-handers More strong left-handers in control group in schizophrenia patients

В				-	
Study name	ratio	Lower	Upper Limit	р	Odds ratio and 95% Cl
Study name Behavioural assessment Gureje 1988 (7) Green et al. 1989 (16) Cannon et al. 1995 (19) Byrne et al. 2004 (38) Behavioural ass. overall Other forms of assessment Wahl 1976 (8) Taylor et al. 1982 (10) Kameyama et al. 1983 (11) Merrin 1984 (13) Green & Rieg 1995 (21) Malesu et al. 1996 (23) Crow et al. 1996 (1) Löw et al. 2000 (29) Baaré et al. 2001 (30) Egan et al. 2001 (30) Egan et al. 2001 (31) Hulshoff Pol et al. 2001 (88) Reilly et al. 2002 (34) Kemether et al. 2003 (35) Upadhyay et al. 2005 (42) Ortuno et al. 2005 (42) Ortuno et al. 2005 (43) Glenthoj et al. 2007 (47) Dane et al. 2009 (49) Bachmann et al. 2010 (51)	0.52 0.78 0.42 0.21 0.50 0.89 1.54 1.03 3.53 1.87 0.55 1.33 0.31 0.75 4.60 0.84 0.52 0.33 0.81 0.75 4.60 0.84 0.52 0.33 0.81 0.75 4.60 0.84 0.52 0.75 1.33 0.31 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.1	Lower Limit 0.01 0.14 0.07 0.01 0.16 0.05 0.70 0.62 0.38 1.01 0.18 0.39 0.01 0.23 1.45 0.44 0.05 0.03 0.07 0.09 0.04 0.25 0.54 0.01 0.67 0.67	26.81 4.41 2.62 4.20 1.55 15.44 3.39 1.72 33.02 3.48 1.67 4.53 8.31 2.46 14.57 1.61 5.38 3.38 9.21 6.28 3.54 3.54 3.54 3.54 3.54 3.54 3.54 3.54	p 0.75 0.78 0.35 0.31 0.23 0.94 0.28 0.91 0.27 0.05 0.29 0.65 0.48 0.63 0.01 0.61 0.58 0.35 0.86 0.35 0.39 0.39 0.20 0.16 0.09 0.42	Odds ratio and 95% CI
Takahashi (personal communication)	5.25	1.03	26.64 1.64	0.43	
Combined	1.18	0.90	1.55	0.23	
					0.01 0.1 1 10 100

Statistics for each study

More strong left-handers More strong left-handers in schizophrenia patients in control group