# Elevated levels of mixed-hand preference in dyslexia: Meta-analyses of 68 studies

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## Abstract

Since almost a hundred years, psychologists have investigated the link between hand preference and dyslexia. We present a meta-analysis to determine whether there is indeed an increase in atypical hand preference in dyslexia. We included studies used in two previous meta-analyses (Bishop, 1990; Eglinton & Annett, 1994) as well as studies identified through PubMed MEDLINE, PsycInfo, Google Scholar, and Web of Science up to August 2022. *K* = 68 studies (*n* = 4660 individuals with dyslexia; *n* = 40845 controls) were entered into three random effects meta-analyses using the odds ratio as the effect size (non-right-handers; left-handers; mixed-handers vs. total). Evidence of elevated levels of atypical hand preference in dyslexia emerged that were especially pronounced for mixed-hand preference (OR = 1.57), although this category was underdefined. Differences in hand skill or strength of hand preference could not be assessed as no pertinent studies were located. Our findings allow for robust conclusions only for a relationship of mixed-hand preference with dyslexia.



**Keywords:** Handedness; dyslexia; laterality; hemispheric asymmetry; reading

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## Introduction

Many cognitive systems are organized asymmetrically (Güntürkün et al., 2020), hence the investigation of alterations in hemispheric asymmetries in psychological disorders and neurodevelopmental conditions has a long tradition in psychological research (Mundorf & Ocklenburg, 2021). One of the most widely investigated learning disability in clinical laterality research, which aims to understand the relationship between physical and mental disorders and brain asymmetries (Mundorf & Ocklenburg, 2022), is dyslexia (Paracchini et al., 2016). Dyslexia is a learning disability that is characterized by difficulties in fluent word reading and/or spelling in the absence of intellectual or sensory deficits (Peterson & Pennington, 2012). It manifests usually early in life from the ages of 5 to 7 as it is mainly diagnosed when children are starting to read and write during (pre-)school (Snowling, 2019).

A postulated link between laterality and dyslexia dates back almost a hundred years to the work of Samuel Torrey Orton. Orton suggested that delayed neurological development leading to a lack of a dominant hemisphere is the cause of developmental dyslexia (Orton, 1925). He moreover claimed that atypical cerebral organization can be reflected through atypical patterns of handedness (i.e., non-right-, left-, and/ or mixed-handedness). Indeed, in the general population, the large majority of individuals (~ 80%) demonstrate a preference for dominantly using their right hand in everyday activities, with the rest 20% of the individuals being about equally divided between left-handers and mixed-handers (Papadatou-Pastou et al., 2020). Thus, a right-hand preference is considered typical. Further historically relevant theories that suggested a link between dyslexia and atypical handedness were the Geschwind-Behan-Galaburda model of cerebral lateralization, which proposed that circulating testosterone levels during gestation delay the development of the language-dominant left hemisphere (Geschwind & Galaburda, 1985a, 1985b, 1985c), and the right-shift theory of Annett (Annett & Kilshaw, 1984), which proposed that a single gene was involved in developing the left hemisphere.

However, substantial criticisms have been brought forward regarding both models (Bryden et al., 1994; McManus et al., 1993). These criticisms did not just pertain to the link between dyslexia and handedness but showed that these theories failed to model cerebral lateralization in general with the emergence of new data on the endocrine and genetic basis for brain asymmetries (Pfannkuche et al., 2009; Wiberg et al., 2019).

Today, the major theoretical approach to the possible relationship between dyslexia and handedness is focused on the genetics of cilia and their role in brain development (Brandler & Paracchini, 2014; Paracchini et al., 2016). Cilia are cell organelles that play a central role in the breaking of left-right asymmetry in the developing embryo, as they generate a leftward flow within the Nodal pathway that is central for left-right axis formation (Hamada, 2020). Interestingly, several dyslexia-related genes are co-expressed in cilia, supporting the idea that similar processes in brain development may affect both structural brain asymmetries and dyslexia risk (Brandler & Paracchini, 2014). Since a recent large-scale study showed that handedness and its genetic determinants are associated with structural brain asymmetries (Sha et al., 2021) it is conceivable that altered asymmetries in brain structure link handedness and dyslexia.

In the published literature, the evidence for a higher prevalence of atypical handedness in individuals with dyslexia is controversial, with some studies reporting effects while others do not (Locke & Macaruso, 1999; Satz & Fletcher, 1987; Vlachos et al., 2013a). To resolve this issue, there have been two attempts to systematically integrate the literature on handedness in dyslexia.

The first attempt was published in a 1990 book by Bishop (1990) and included data from 25 case-control studies on handedness (as measured via hand preference) and dyslexia that had been published between 1932 (Monroe, 1932) and 1987 (Felton et al., 1987). A count of significant results revealed that in two out of the 25 studies, the comparison between individuals with dyslexia and controls reached significance at the $p<0.05$ level. Integration of the data revealed that 11.3% of individuals with dyslexia and 10.6% of controls were left-handed, a non-significant result. The author then conducted a second analysis in which the study with the largest sample size was removed, as it showed a reversed result pattern and may have had a disproportionately large influence on the result of the first analysis. In this analysis, 11.2% of individuals with dyslexia and 5.8% of controls were left-handed. This difference was significant, but it is noteworthy that it seemed to have been driven by a reduction of left-hand preference prevalence in controls compared to the first analysis, not an increase of left-hand preference in individuals with dyslexia. The author concluded that the prevalence of left-hand preference in individuals with dyslexia may be up to twice of the prevalence in controls.

Four years later, the same dataset was re-examined in a second publication by Eglinton and Annett (1994) but with a different methodological approach. In this study, the authors performed two meta-analyses comparing individuals with dyslexia and controls (right-handed versus mixed-handed and left-handed combined, and left-handed versus mixed-handed and right-handed combined) following an established protocol for meta-analysis (Rosenthal, 1991). Specifically, the authors determined a 2×2 $\chi^2$ for each study and then determined a $Z$ score for each study based on the $\chi^2$ statistic. They then added the $Z$ scores to obtain overall significance for the two comparisons. For the RH versus MH and LH combined meta-analysis, the overall $Z$ was 4.36 with $p < .0001$. For the LH versus MH and RH combined meta-analysis the overall $Z$ was 2.93 with a $p = .0017$. Thus, both effects reached statistical significance in the direction expected by the authors, indicating a higher number of non-right-handed individuals with dyslexia compared to controls.

Both attempts at integrating data on hand preference and dyslexia are more than 25 years old by now and several dozen new studies on the topic have been published in the meantime (see table 1 in the methods section). Importantly, recent large-scale studies had substantially more participants than earlier studies, with one of them including thousands of participants (Abbondanza et al., 2023). Integrating these new studies will thus make the findings on hand preference and dyslexia decidedly more robust than the earlier integration attempts. Moreover, the best practice for meta-analysis has substantially changed in the last two decades. Non-weighted approaches or adding up *Z* scores is not the preferred method for comparing cases and controls anymore. In contrast, random-effects meta-analysis based on the odds ratio (OR) as the effect size index is considered best practice for this research question today (Harrer et al., 2021).

In comparison with $\chi^2$, the main advantage of the OR is the calculation of the combined effect, which is the combined of the effects from the included studies, weighted according to study size. Smaller studies (studies with smaller participant sample sizes), contribute less than large studies, because smaller studies are more subject to effects occurring by chance (Rosenthal & DiMatteo, 2001). Furthermore, the OR is independent of the base rate of the event in question. For example, in the present study the OR could be affected by the handedness instrument or the cut off criteria used to determine non-right-handedness. Additionally, modern meta-analytic procedures give the opportunity for assessing the presence of heterogeneity between studies and for explaining this heterogeneity via moderator variable analysis as well as for estimating the presence of small study bias, which could be due to factors such as poorer methodological quality of smaller studies, or due to publication bias. Publication bias can distort findings because studies with statistically significant results are more likely to get published than studies without significant results. Indeed, a number of recent, large-scale meta-analyses on the relationship between hand preference and other learning difficulties (e.g., mathematical learning difficulties (Papadatou-Pastou et al., 2021)), neurodevelopmental disorders (attention deficit hyperactivity disorder (Nastou et al., 2022) and autism (Markou et al., 2017a)) and psychiatric disorders (e.g., post-traumatic stress disorder (Borawski et al., 2023) and depression (Packheiser et al., 2021)) have used the odds ratio as their effect size.

The purpose of the present study is to compare hand preference in individuals with dyslexia and controls using state-of-the-art meta-analytic techniques to provide a more reliable and precise overall result. Ascertaining potential differences between individuals with dyslexia and healthy controls has potential implications for academics, clinicians as well as the general population. For researchers, understanding the ontogenesis and genetic basis of handedness can be studied especially well in individuals where the development of handedness is atypical. For clinicians, educators and parents, finding potential biomarkers of dyslexia during development could aid in early identification and diagnostics, which would in turn allow for early intervention. Therefore, we aimed to determine the effect size of the difference between the two groups, as well as assess the presence of heterogeneity (and explain it through moderator analysis), and investigate the presence of small study bias and publication bias. Furthermore, we updated the database with studies that were published between 1994 and 2022. Based on the previous literature on this topic, we hypothesize that individuals with dyslexia show higher rates of atypical hand preference than controls.

## Methods

### *Transparency and Openness*

The meta-analyses were conducted following the PRISMA statement (Page et al., 2021). The PRISMA 2020 Main Checklist as well as the PRISMA 2020 Abstract Checklist are to be found in the Supplementary Material. The study was not preregistered. All data and code for analysis are available under the following link: https://osf.io/waqj4/?view_only=c21a6f7342fd47f8b1eb572945e31c50.

### *Search strategy*

The studies that were included into the present meta-analyses were (a) the 21 studies that were previously also included in Bishop (1990) as well as in Eglinton & Annett (1994) and (b) 47 studies that were published between 1987 and 2022 (see table 1 for all studies). Note that not all studies included in Bishop (1990) were included in the present analysis, due to different inclusion / exclusion criteria.

***Table 1***: *Studies included in the meta-analysis including hand preference distributions and moderators. Details on moderators are given in the statistical analysis section. L-R = Left-Right, L-M-R = Left-Mixed-Right, NR-R = Non-right-Right. EHI = Edinburgh Handedness Inventory. * = study with unclear IQ criterion. Note that the study of Abbondanza et al. (2023) was included in the search until 2022 since a preprint was published in 2022.*

| Study | Non-right Dyslexia | Non-right Control | Left Dyslexia | Left Control | Mixed Dyslexia | Mixed Control | Classification System | Inventory | Sex Ratio | Mean Age | Diagnostic Method | Location | IQ Cut-off |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Abbondanza et al. (2023)** | *138* | *275* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *other* | *3.11* | *NA* | *yes* | *Europe* | *85* |
| **Annett & Kilshaw (1984)** | *66* | *551* | *9* | *47* | *57* | *504* | *L-M-R* | *Annett* | *0.82* | *12.00* | *no* | *Europe* | *NA* |
| **Annett et al. (1996)** | *3* | *33* | *3* | *33* | *NA* | *NA* | *L-R* | *NA* | *0.99* | *NA* | *no* | *Europe* | *NA* |
| **Bakos et al. (2017)** | *3* | *5* | *3* | *5* | *NA* | *NA* | *L-R* | *other* | *0.73* | *8.15* | *no* | *Europe* | *85* |
| **Bakos et al. (2020)** | *6* | *6* | *6* | *6* | *NA* | *NA* | *L-R* | *other* | *0.97* | *10.26* | *no* | *Europe* | *85* |
| **Banfi et al. (2021)** | *3* | *3* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *NA* | *1.33* | *9.40* | *no* | *Europe* | *85* |
| **Barkus et al. (2022) *** | *10* | *5* | *4* | *4* | *6* | *1* | *L-M-R* | *other* | *0.39* | *25.40* | *yes* | *Europe* | *NA* |
| **Best & Demb (1999)** | *0* | *1* | *0* | *1* | *NA* | *NA* | *L-R* | *other* | *1.50* | *NA* | *NA* | *North America* | *NA* |
| **Bettman (1967)** | *7* | *7* | *6* | *6* | *1* | *1* | *L-M-R* | *other* | *1.56* | *10.50* | *yes* | *North America* | *NA* |
| **Bishop (1984)** | *23* | *1160* | *23* | *1160* | *NA* | *NA* | *L-R* | *other* | *NA* | *NA* | *no* | *Europe* | *NA* |
| **Boets et al. (2007)** | *4* | *3* | *4* | *3* | *NA* | *NA* | *L-R* | *other* | *1.40* | *NA* | *no* | *Europe* | *NA* |
| **Bradshaw et al. (2020) *** | *7* | *2* | *7* | *2* | *NA* | *NA* | *L-R* | *other* | *NA* | *22.74* | *no* | *Europe* | *NA* |
| **Bradshaw et al. (2021) *** | *9* | *2* | *8* | *2* | *1* | *0* | *L-R* | *other* | *NA* | *NA* | *no* | *Europe* | *NA* |

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| **Braun et al. (2000) *** | *11* | *7* | *11* | *7* | *NA* | *NA* | *L-R* | *NA* | *2.26* | *NA* | *NA* | *Europe* | *NA* |
| **Brem et al. (2020)** | *7* | *14* | *7* | *14* | *NA* | *NA* | *L-R* | *NA* | *1.10* | *9.97* | *no* | *Europe* | *85* |
| **Caccia & Lorusso (2020)** | *1* | *1* | *1* | *1* | *NA* | *NA* | *L-R* | *NA* | *2.44* | *12.40* | *yes* | *Europe* | *85* |
| **Di Folco et al. (2022)** | *126* | *3334* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *other* | *1.04* | *NA* | *no* | *Europe* | *77.5* |
| **Doehring (1968)** | *5* | *7* | *5* | *7* | *NA* | *NA* | *L-R* | *NA* | *NA* | *NA* | *NA* | *NA* | *NA* |
| **Elsherif (2020)** | *31* | *9* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *other* | *0.44* | *20.39* | *no* | *Europe* | *NA* |
| **Felton et al. (1987)** | *5* | *7* | *5* | *7* | *NA* | *NA* | *L-R* | *NA* | *5.13* | *NA* | *no* | *North America* | *85* |
| **Fraga González et al. (2018)** | *3* | *1* | *3* | *1* | *NA* | *NA* | *L-R* | *EHI* | *0.56* | *22.62* | *no* | *Europe* | *NA* |
| **Fraga González et al., (2016a)** | *2* | *2* | *2* | *2* | *NA* | *NA* | *L-R* | *other* | *1.00* | *7.96* | *no* | *Europe* | *85* |
| **Fraga González et al., (2016b)** | *3* | *2* | *3* | *2* | *NA* | *NA* | *L-R* | *other* | *0.73* | *7.06* | *no* | *Europe* | *85* |
| **Gates & Bond (1936)** | *7* | *6* | *2* | *2* | *5* | *4* | *L-M-R* | *other* | *NA* | *8.61* | *NA* | *North America* | *80* |
| **Gross et al. (1978)** | *3* | *0* | *3* | *0* | *NA* | *NA* | *L-R* | *other* | *6.25* | *12.11* | *no* | *North America* | *90* |
| **Hallgren, (1950)** | *33* | *23* | *33* | *23* | *NA* | *NA* | *L-R* | *NA* | *NA* | *NA* | *NA* | *NA* | *NA* |
| **Hari et al. (2001) *** | *0* | *2* | *0* | *1* | *0* | *1* | *L-M-R* | *NA* | *0.92* | *NA* | *no* | *Europe* | *NA* |
| **Harris (1957)** | *50* | *115* | *7* | *9* | *43* | *106* | *L-M-R* | *other* | *NA* | *8.00* | *yes* | *Europe* | *80* |
| **Hashimoto et al. (2020)** | *3* | *2* | *3* | *2* | *NA* | *NA* | *L-R* | *EHI* | *5.36* | *10.70* | *no* | *Asia* | *70* |

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| **Hazzaa et al. (2021)** | *3* | *1* | *3* | *1* | *NA* | *NA* | *L-R* | *NA* | *1.61* | *7.97* | *no* | *Africa* | *90* |
| **Heim et al. (2003a)** | *2* | *2* | *0* | *0* | *2* | *2* | *L-M-R* | *EHI* | *1.22* | *NA* | *NA* | *NA* | *NA* |
| **Heim et al. (2003b)** | *1* | *1* | *1* | *0* | *0* | *1* | *L-M-R* | *EHI* | *1.60* | *NA* | *NA* | *Europe* | *85* |
| **Illingworth & Bishop (2009)** | *5* | *3* | *5* | *3* | *NA* | *NA* | *L-R* | *EHI* | *0.50* | *NA* | *yes* | *Europe* | *NA* |
| **Jariabková et al. (1995)** | *16* | *10* | *7* | *4* | *9* | *6* | *L-M-R* | *other* | *NA* | *NA* | *yes* | *Europe* | *90* |
| **Kronschnabel (2016)** | *3* | *4* | *2* | *4* | *1* | *0* | *L-M-R* | *EHI* | *1.06* | *15.97* | *no* | *Europe* | *NA* |
| **Kühn et al. (2021) *** | *3* | *3* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *other* | *0.50* | *19.00* | *yes* | *Europe* | *NA* |
| **Leppänen et al. (2019)** | *20* | *28* | *17* | *25* | *3* | *3* | *L-M-R* | *Annett* | *1.61* | *10.06* | *NA* | *Europe* | *85* |
| **Liddle et al. (2009)** | *0* | *5* | *0* | *5* | *NA* | *NA* | *L-R* | *EHI* | *0.47* | *NA* | *no* | *Europe* | *NA* |
| **Locke & Macaruso (1999) *** | *43* | *64* | *43* | *64* | *NA* | *NA* | *L-R* | *other* | *2.14* | *NA* | *no* | *North America* | *NA* |
| **Ma et al. (2015)** | *0* | *0* | *0* | *0* | *NA* | *NA* | *L-R* | *other* | *1.06* | *12.10* | *no* | *North America* | *85* |
| **Malmquist (1958)** | *4* | *21* | *1* | *4* | *3* | *17* | *L-M-R* | *NA* | *NA* | *NA* | *no* | *Europe* | *90* |
| **Martins et al. (2021)** | *3* | *2* | *2* | *0* | *1* | *2* | *L-M-R* | *EHI* | *0.57* | *8.19* | *no* | *Europe* | *NA* |

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| **Mehlhase et al. (2020)** | *3* | *5* | *3* | *5* | *NA* | *NA* | *L-R* | *other* | *1.06* | *10.15* | *no* | *Europe* | *85* |
| **Monroe (1932)** | *14* | *11* | *14* | *11* | *NA* | *NA* | *L-R* | *NA* | *NA* | *NA* | *NA* | *NA* | *NA* |
| **Naidoo (1972)** | *44* | *22* | *10* | *5* | *34* | *17* | *L-M-R* | *NA* | *NA* | *NA* | *NA* | *NA* | *NA* |
| **Paul et al. (2006) *** | *10* | *1* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *NA* | *2.18* | *NA* | *no* | *Europe* | *NA* |
| **Pennington et al. (1987)** | *15* | *15* | *1* | *2* | *14* | *13* | *L-M-R* | *EHI* | *NA* | *NA* | *no* | *North America* | *NA* |
| **Polikoff et al. (1995)** | *12* | *7* | *2* | *5* | *10* | *2* | *L-M-R* | *other* | *NA* | *NA* | *NA* | *Europe* | *NA* |
| **Prior et al. (1983)** | *3* | *2* | *1* | *0* | *2* | *2* | *L-M-R* | *NA* | *NA* | *11.00* | *NA* | *Australia* | *NA* |
| **Rae et al. (2002)** | *3* | *3* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *Annett* | *NA* | *NA* | *yes* | *Australia* | *NA* |
| **Renvall et al. 2005)** | *0* | *1* | *0* | *0* | *0* | *1* | *L-M-R* | *NA* | *0.60* | *NA* | *yes* | *Europe* | *86* |
| **Rezvani et al. (2019)** | *2* | *2* | *2* | *2* | *NA* | *NA* | *L-R* | *other* | *1.00* | *8.29* | *no* | *Europe* | *NA* |
| **Richardson (1994)** | *29* | *20* | *6* | *4* | *23* | *16* | *L-M-R* | *Annett* | *1.32* | *NA* | *yes* | *Europe* | *NA* |
| **Rippon & Brunswick (2000)** | *3* | *1* | *3* | *1* | *NA* | *NA* | *L-R* | *Annett* | *2.73* | *NA* | *no* | *Europe* | *NA* |
| **Robichon & Habib (1998)** | *7* | *2* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *EHI* | *NA* | *NA* | *yes* | *Europe* | *90* |
| **Ruff et al. (2002)** | *1* | *1* | *1* | *1* | *NA* | *NA* | *L-R* | *EHI* | *NA* | *NA* | *NA* | *Europe* | *NA* |
| **Rutter et al. (1970)** | *21* | *31* | *8* | *7* | *13* | *24* | *L-M-R* | *NA* | *NA* | *NA* | *NA* | *NA* | *NA* |

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| **Samara & Caravolas (2017) *(Experiment 1)*** | *5* | *6* | *5* | *6* | *NA* | *NA* | *L-R* | *other* | *0.67* | *20.61* | *no* | *Europe* | *80* |
| **Samara & Caravolas (2017) *(Experiment 2)*** | *4* | *3* | *3* | *3* | *1* | *0* | *L-M-R* | *other* | *0.70* | *20.58* | *no* | *Europe* | *80* |
| **Schevill (1980)** | *15* | *7* | *12* | *7* | *3* | *0* | *L-M-R* | *NA* | *NA* | *NA* | *NA* | *NA* | *NA* |
| **Schonell (1941)** | *10* | *5* | *10* | *5* | *NA* | *NA* | *L-R* | *other* | *NA* | *NA* | *NA* | *NA* | *70* |
| **Serrallach et al. (2016)** | *3* | *4* | *3* | *4* | *NA* | *NA* | *L-R* | *other* | *0.46* | *5.46* | *yes* | *Europe* | *80* |
| **Siviero et al. (2002) *** | *2* | *0* | *2* | *0* | *NA* | *NA* | *L-R* | *other* | *1.07* | *NA* | *no* | *South America* | *NA* |
| **Skeide et al. (2016)** | *2* | *12* | *2* | *4* | *0* | *8* | *L-M-R* | *EHI* | *1.47* | *6.40* | *no* | *Europe* | *85* |
| **Skeide et al. (2018)** | *1* | *2* | *0* | *1* | *1* | *1* | *L-M-R* | *other* | *NA* | *NA* | *yes* | *Europe* | *85* |
| **Smith (1950)** | *4* | *7* | *4* | *7* | *NA* | *NA* | *L-R* | *NA* | *NA* | *10.00* | *NA* | *NA* | *NA* |
| **Stella (2018) *** | *NA* | *NA* | *5* | *6* | *NA* | *NA* | *L-NL* | *other* | *0.27* | *21.01* | *yes* | *Europe* | *NA* |
| **Sturm et al. (2021)** | *4* | *0* | *4* | *0* | *NA* | *NA* | *L-R* | *NA* | *1.08* | *10.38* | *yes* | *North America* | *NA* |
| **Tamboer et al. (2015) *** | *6* | *8* | *6* | *8* | *NA* | *NA* | *L-R* | *other* | *0.16* | *20.44* | *no* | *Europe* | *NA* |
| **Tamboer et al. (2016) *** | *8* | *54* | *4* | *39* | *4* | *15* | *L-M-R* | *other* | *0.33* | *19.76* | *yes* | *Europe* | *NA* |
| **van de Walle de Ghelcke et al. (2021)** | *3* | *3* | *3* | *3* | *NA* | *NA* | *L-R* | *other* | *1.00* | *14.10* | *yes* | *Europe* | *NA* |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **(Van Der Lubbe et al., (2019) *** | *1* | *0* | *1* | *0* | *NA* | *NA* | *L-R* | *Annett* | *1.36* | *NA* | *NA* | *Europe* | *NA* |
| **Van Setten et al. (2016) *** | *12* | *3* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *other* | *0.25* | *22.30* | *yes* | *Europe* | *NA* |
| **van Setten et al. (2019)** | *3* | *7* | *3* | *7* | *NA* | *NA* | *L-R* | *other* | *0.75* | *12.23* | *no* | *Europe* | *80* |
| **Velay et al. (2002)** | *5* | *5* | *NA* | *NA* | *NA* | *NA* | *NR-R* | *EHI* | *1.80* | *NA* | *no* | *Europe* | *90* |
| **Vlachos et al. (2013a)** | *10* | *9* | *8* | *5* | *2* | *4* | *L-M-R* | *EHI* | *3.09* | *NA* | *yes* | *Europe* | *80* |
| **Williams et al. (2018)** | *5* | *7* | *5* | *7* | *NA* | *NA* | *L-R* | *other* | *1.00* | *10.87* | *no* | *North America* | *70* |
| **Wolf & Goodglass (1986)** | *0* | *7* | *0* | *7* | *NA* | *NA* | *L-R* | *other* | *1.28* | *8.23* | *no* | *North America* | *NA* |
| **Wolfe (1941)** | *5* | *2* | *4* | *2* | *1* | *0* | *L-M-R* | *other* | *NA* | *9.50* | *NA* | *North America* | *NA* |
| **Wussler & Barclay (1970)** | *3* | *1* | *3* | *1* | *NA* | *NA* | *L-R* | *other* | *NA* | *10.65* | *NA* | *North America* | *NA* |
| **Zaric (2016)** | *3* | *3* | *3* | *3* | *NA* | *NA* | *L-R* | *Annett* | *1.35* | *9.12* | *no* | *Europe* | *85* |
| **Žarić et al. (2017)** | *6* | *2* | *6* | *2* | *NA* | *NA* | *L-R* | *other* | *1.04* | *8.75* | *no* | *Europe* | *85* |

The new studies were located through an online search in the computerized reference databases PubMed MEDLINE, PsycInfo, Google Scholar, and Web of Science using the search term (*handedness* OR *hand preference* OR *laterality* OR *hand skill)* AND (*dyslexia* OR *developmental reading disorder* OR *reading disability)* in "All Fields" and limiting the year of publication from 1987 to 2022. The cited literature of all articles that were eligible for inclusion was scanned, and as more papers were obtained, their references were searched for potentially eligible articles as well. In addition, e-mail requests for unpublished data were sent to the authors of the articles (when e-mail addresses could be retrieved). If studies clearly measured hand preference but incidences were not reported (e.g., if they were only used as a covariate in a larger model), the authors were contacted to obtain raw data. The search strategy aimed for completeness.

*Study Selection*

*Inclusion and exclusion criteria*

Studies were included if (i) participants were diagnosed with dyslexia and (ii) if hand preference information was reported. Inclusion of an individual study in the meta-analysis was further subject to the following inclusion and exclusion criteria:

1. IQ: Studies were excluded if they did not give information about the IQ of the participants. To be included in the meta-analysis, studies had to include participants with IQ $\geq 70$. The cut-off was chosen as an IQ of less than 70 is defined as an intellectual disability according to DSM-V criteria (American Psychiatric Association, 2013). A total of 14 studies were excluded as they did not make a specific statement on IQ or left it unclear if individuals were below the IQ threshold (see Table 1 where these studies are marked with an asterisk). As it was still likely that these studies tested dyslexic samples above the IQ threshold --as dyslexia cannot be diagnosed in the presence of an intellectual disability-- we added these studies in additional exploratory analyses. Of note, these studies were only included to explore their influence on the overall results of each meta-analysis. For sub-analyses of moderators, small study bias, or publication bias, these studies were not included.
2. Reading disability criterion: Studies had to report some indication that reading level was well below mental age or chronological age. Studies in which the criterion for reading disability was not specific were excluded. For example, in the Abrams and colleagues study (Abrams et al., 2009), children were defined as poor readers if they

were at the bottom third in a reading test out of a total of 23 participants. Thus, this study was excluded.

3. Dyslexia status: Studies that excluded individuals with dyslexia were excluded. Studies which only ascertained the risk to develop dyslexia and not the presence of dyslexia per se were excluded (e.g., Louleli and colleagues (2020)). Participants who met the criterion for dyslexia were referred to in the original articles using a large number of terms suggesting heterogeneity in the labeling of this learning disorder. This terminology includes, but is not exhaustive to, dyslexics (e.g., Hazzaa and colleagues (2021)), developmental dyslexics (e.g., Heim and colleagues (2003b)), retarded readers (e.g., Smith (1950)), reading disabled (e.g., Felton and colleagues (1987)), children with reading disability (e.g., Wussler & Barclay (1970)), children with reading deficits (e.g., Mehlhase and colleagues (2020)), specific reading retarded (e.g., Annett & Kilshaw (1984); Bishop (1990)), reading retarded (Naidoo (1972)), or severely impaired readers (e.g., Wolf & Goodglass (1986)).
4. Control group: Studies without a control group of typically developing individuals were excluded.
5. Selection for hand preference: Studies were excluded if participants were selected on the basis of their hand preference, typically to match the hand preference of individuals with dyslexia to controls (e.g., Dufor and colleagues (2007)) or to include only right-handers (e.g., Best & Demb (1999)). Studies that balanced for handedness by including equal numbers of for example left- and right-handed individuals were also excluded.
6. Sufficient hand preference data: Hand preference had to be presented in a way that allows to extract a frequency for individuals with dyslexia and controls separately. If no information on handedness was provided, the study was excluded. If only lateralization quotients were presented without hand preference frequencies, the study was excluded as this variable was reported too rarely for further analysis.
7. Publication language: Reports had to be written in English, Greek or German. Only English studies were found, however.
8. Duplicate datasets: In case studies reported duplicates from previously reported datasets (e.g., Kibby and colleagues (2004), Parmar and colleagues (2021), and Renvall & Hari (2003)), the duplicate dataset was excluded.
9. Publication type: No case studies of individuals with dyslexia were included. Review studies were also excluded.

Studies were included even if hand preference was reported as an incidental finding or to describe participants, rather than being the main focus of the study. Details about the method of literature search and study selection are shown in Figure 1.

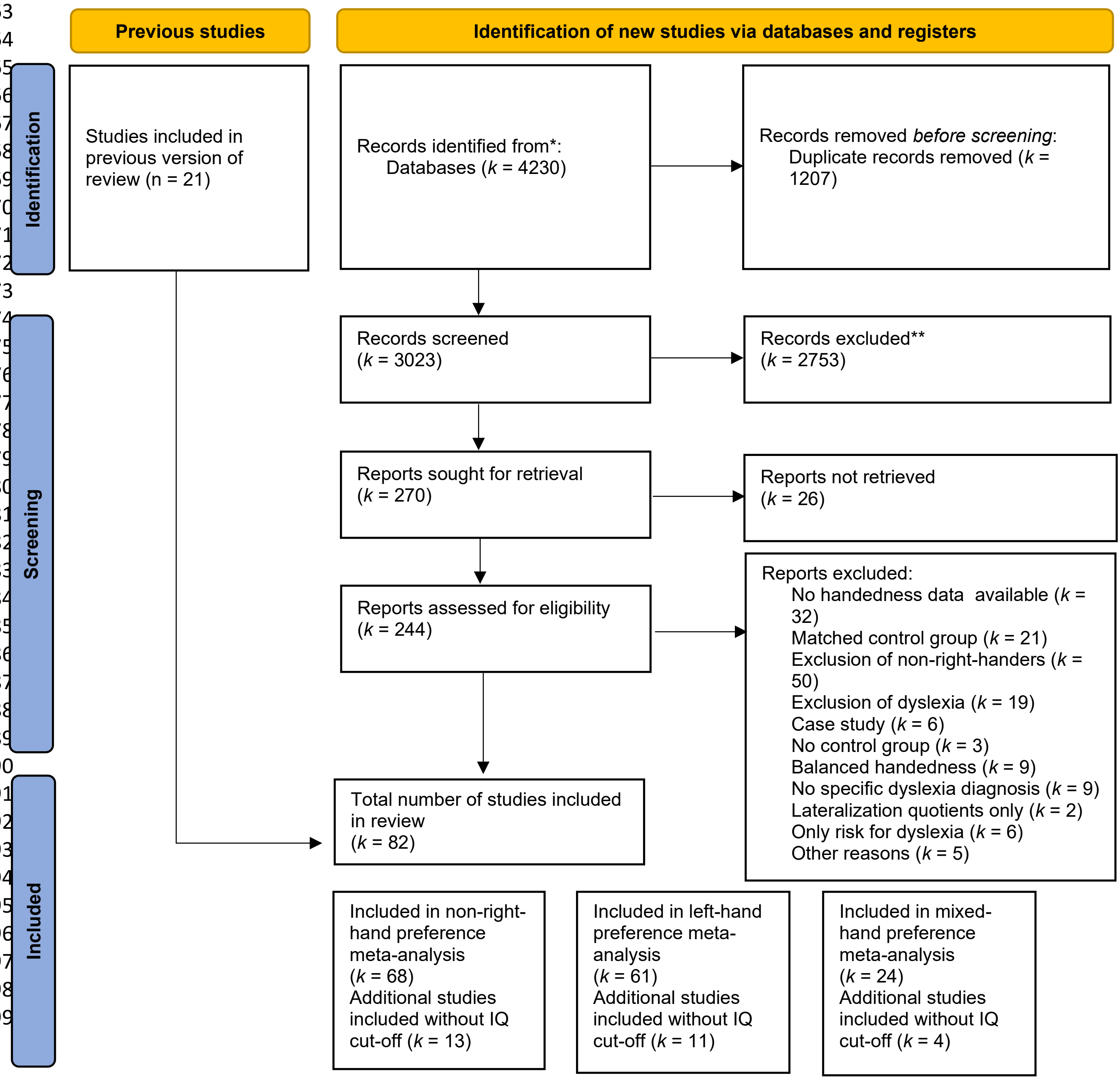

Figure 1. Flow chart for the literature search. The search was conducted in accordance with the updated PRISMA guidelines *(Page et al., 2021)*.

*Data extraction*

Data extraction was performed after records were deemed eligible for inclusion after first reviewing the abstract and then the full-text by at least two authors (MPP and AK for the search until June 2015, CS and JP for the other searches). Study selection and inconsistencies were resolved by discussion. Data extraction was performed by MPP, AK, CS, JP, and JS. Data from each study was extracted by at least two raters. Interrater reliability was very high (Cohen's $\kappa > 0.9$). Any inconsistencies were resolved through discussion. Data collection and extraction was conducted in two steps, i.e. first until June 2015 by MPP and AK and second until October 2022 by CS, JP, and JS. During extraction, the number of left-, mixed-, or non-right-handed individuals as well as the overall number of participants in the study were extracted for individuals with dyslexia and their respective control group. We only extracted frequencies of left-, mixed- or non-right-hand preferences rather than continuous measures such as lateralization quotients as frequencies were reported in the large majority of cases only. It should be noted that mixed-hand preferences in our study reflect an umbrella term that comprises a third, "middle" category comprising both ambidexterity (no hand preference within a task) and inconsistent hand use (using different hands across different activities). In addition, we extracted the tool for handedness assessment, the number of male and female individuals in the sample, the average age of the sample, the method of diagnosing dyslexia, the location in which the study was conducted, and the IQ cut-off criterion used in the study. Mixed-hand preferences as defined in our meta-analysis were diversely characterized across studies. From the k = 28 studies included in this analysis, k = 13 studies mentioned to have measured ambidexterity and k = 5 studies measured inconsistent hand use. The other studies measured mixed-hand preference without further definition.

*Statistical analysis*

Data were analyzed using R (v. 4.2.2 for Windows) and RStudio (2022.07.2 Build 576; R Core Team 2022) using the metafor package (Viechtbauer, 2010) and the RoBMA package (Maier et al., 2022) to calculate both frequentist random-effects and robust Bayesian meta-analyses. In total, we conducted three meta-analyses that differed in terms of study inclusivity due to different classification systems, following previous work (Borawski et al., 2023; Markou et al., 2017b; Nastou et al., 2022; Packheiser et al., 2021).

(i) First, we investigated whether the prevalence of non-right-hand preference differed between individuals with dyslexia and controls. To this end, we compared the extracted frequencies of non-right-hand preferences in individuals with dyslexia with their respective control group. All included studies but one (Stella, 2018) could be converted to a NR-R classification by assigning left-handers from the L-R classification and left- and mixed-handers from the L-M-R classification into the non-right category.

(ii) In a second meta-analysis, we excluded seven studies that exclusively used a NR-R classification to investigate differences in the prevalence of left-hand preference between individuals with dyslexia and controls leaving 61 studies for analysis. Thus, individuals that were classified as left-handed for studies employing an L-R or an L-M-R classification were included in the second meta-analysis. The study of Stella (2018) that used a Non-left-Left criterion was also included here. As for the first meta-analysis, we compared the frequencies of left-hand preferences in individuals with dyslexia with their respective control group.

(iii) In the third meta-analysis, we investigated differences in the prevalence of mixed-hand preference between individuals with dyslexia and controls. For this purpose, 44 studies needed to be excluded that did not classify individuals into a mixed-hand preference category leaving 24 studies for analysis. Identical to meta-analysis (i) and (ii), we compared the frequencies of mixed-hand preferences in individuals with dyslexia with their respective control group.

We used odds ratios (ORs) as the effect size measure in all three meta-analyses. ORs are defined as the ratio of the odds of an event occurring in one group (i.e., individuals with dyslexia) relative to the odds of the event occurring in another group (i.e., controls). In this case, the events refer to non-right-hand preference (meta-analysis 1), left-hand preference (meta-analysis 2), or mixed-hand preference (meta-analysis 3). ORs and their corresponding 95% confidence intervals (CI) were calculated for each data set independently. An OR equal to 1 would indicate no difference between individuals with dyslexia and controls, thus support the null hypothesis. An OR greater or less than 1 would indicate increased or decreased rates of atypical hand preference in individuals with dyslexia compared to controls, respectively. In contrast to relative proportions of event rates in the population, ORs are not immediately understood however without taking the basic event rate in the population into account. For example, the OR for increases in left-hand preference in males compared to females is 1.23

indicating that it is 23% more likely for males to be left-handed compared to females. Since the event rate of females exhibiting left-hand preference in the population is only 10%, this 23% increase results in a total proportion (PP) of around 12% in males. For this reason, we also transformed ORs into simple proportions using the following formula:

$$\text{Individuals with Dyslexia PP} = \frac{Controls\ PP * OR}{1+Controls\ PP * \ (OR-1)}$$

We calculated the corresponding variance of the ORs for each dataset independently using the escalc function in the metafor package. ORs and their variances were then combined using a random effects model to provide a pooled effect size and a test for the overall effect. We exclusively used random-effects models as previous research has demonstrated that there is abundant variability in the hand preference measures used as well in the ways that reading disability is assessed. ORs were tested for significance using classical frequentist approaches providing *p*-values and z-values as indicators of significance and effect size as well as robust Bayesian approaches. Both frequentist and Bayesian analyses were performed one-tailed due to our directional hypotheses. Bayesian approaches have the advantage of quantifying evidence for the null as well as for the alternative hypothesis. For interpretation of the Bayes factors, we used the terminology and guidelines established by Lee and Wagenmakers (2014) where a $BF_{10}$ of $> 3$ represents moderate evidence in favor of the alternative hypothesis, i.e. that there are increased rates of atypical hand preference between individuals with dyslexia and controls, and where a $BF_{10}$ of $< 0.33$ represents moderate evidence in favor of the null hypothesis, i.e. that there is no difference between individuals with dyslexia and controls. $BF_{10}$ values of one suggest that there is an absence of evidence. For Bayesian meta-analyses, ORs were transformed into Cohen's *d* as a measure of effect size. Recent literature has suggested the use of a sensitivity approach and thus a variety of priors to provide a more comprehensive picture of the data (Harrer et al., 2021). As suggested by Harrer and colleagues (2021), effect sizes in meta-analyses are typically low suggesting the usage of small effect size priors. We thus used a scaling factor of $d = 0.3$ as an initial effect prior. This was complemented with robustness analyses using $d = 0.5$ (medium effect) and $d = 0.707$ (default prior in JASP and average effect size in cognitive neuroscience (Szucs & Ioannidis, 2017). All priors were located at 0 and followed a truncated half-Cauchy distribution that is generally recommended in Bayesian approaches (Ghosh et al., 2018). Results for the sensitivity analyses can be found in Supplementary Table 1.

Heterogeneity in each meta-analysis was assessed using Cochran's *Q,* statistic, the $I^2$ and the $\tau^2$ index. These provide complementary information on between-study variation. The *Q* statistic is used to determine whether the primary level effect sizes estimate a common population effect size. The $I^2$ index reflects the percentage of beyond-chance level variation across studies that can be attributed to heterogeneity and the $\tau^2$ index is an estimate of the between-studies variance. Significance of heterogeneity was assessed based on the *Q* statistic and supported through a Bayes factor using default priors of the RoBMA function. In the case of heterogeneity, moderator analyses were performed to determine if the outlined moderators were associated with the between-study variance. The threshold to conduct moderator analyses was either a significant *Q* statistic, an $I^2$ value above 25% (Higgins et al., 2003) or a $BF_{10} > 3$. For categorical moderators, the intercept was removed from the analysis for interpretation of all factor levels. The following moderators were tested:

*Year of publication*: The prevalence of atypical hand preference has been shown to be moderated by secular change as studies published prior to 1976 demonstrate a decreased prevalence of left-hand preference in the population compared to later studies (Papadatou-Pastou et al., 2020), possibly due to cultural tendencies that forced a right-hand use in schools in earlier time periods (de Kovel et al., 2019). Publication year was used as a continuous meta-regressor in our study and was extracted numerically for all eligible studies.

*Classification of hand preference:* Studies included in our meta-analyses were categorized into three classification systems that were typically employed in the included studies. The most common classification system was the Left-Right (L-R) classification (37 studies) that used a binary classification to divide individuals either into left- or right-handers. The next most used classification system was the Left-Mixed-Right (L-M-R) classification system that divided participants into left-handers, mixed-handers/ambidextrous individuals (here collectively referred to as "mixed-handers"), or right-handers (24 studies). The least common category in our datasets was the Non-Right/Right (NR-R) classification (7 studies). In this category, left-handers and mixed-handers were subsumed under not-being right-handed and could thus not be disambiguated for further analyses of left- or mixed-hand preference. A single study employed multiple classification systems (Vlachos et al., 2013b), that is a binary L-R system, a 3-way L-M-R system, and a 5-way classification that differentiated between strong and moderate left- and right-hand preference as well as mixed-hand preference. As this was only an isolated case, we used the 3-way classification of this study in the present analyses.

*Hand preference assessment:* The method of assessing hand preference has shown to influence the classification rates into left- or right-hand preference with self-reports resulting in slightly lower levels of left-hand preference compared to handedness inventories (Papadatou-Pastou et al., 2020). The studies were thus coded for instrument representing the two most common instruments used to measure hand preference in the present data set, namely the Annett's Handedness Questionnaire (Annett, 1970), 10 studies) and the Edinburgh Handedness Inventory (Oldfield, 1971), 14 studies). Due to the large diversity of other methods of assessing hand preference, they were grouped in a one larger subgroup (32 studies).

*Sex ratio:* The relative proportion of left-handed females compared to right-handed females in the population is estimated to be 10% whereas this proportion is 12% for males (Papadatou-Pastou et al., 2008). Thus, we aimed to investigate sex differences as a moderator in the present meta-analyses. Unfortunately, possible sex differences could not be directly investigated as the included studies for the most part did not break down their results by sex, as for example done by Annett and Kilshaw (Annett & Kilshaw, 1984). The sex ratio was calculated as follows:

$$\text{Sex ratio} = \frac{Number\ of\ males\ in\ cohort}{Number\ of\ females\ in\ cohort}$$

A value of 1 thus indicates that the sample comprised males and females in equal numbers whereas as value of 2 reflects that there were twice as many males in the sample compared to females. Sex ratio as a moderator was extracted for 45 studies.

*Age:* As dyslexia and control cohorts were largely matched for age, we used the mean age of the entire cohort as a continuous meta-regressor.

*Location:* Study location was assessed to approximate ancestry of the sample, as ancestry has been shown to moderate the overall hand preference prevalence. For example, individuals of European ancestry show higher rates of left-hand preference compared to individuals of Asian ancestry (Papadatou-Pastou et al., 2020). Studies were categorized for this analysis into North American (12 studies), South American (0 studies), European (46 studies), Asian (2 studies), African (1 study) and Oceanian (1 study) study location in accordance with previous work (Packheiser et al., 2020).

*Diagnostic method:* The assessment of dyslexia across studies was highly heterogeneous using a large number of psychometric tests that differed from study to study and especially from language to language. We thus decided to use a binary classification grouping together studies in which individuals were diagnosed by a trained psychologist (15 studies) and studies that solely relied on psychometric tests for the assessment of dyslexia (33 studies).

*IQ cut-off:* The cut-off for IQ values varied from study to study ranging from 70 to 90. We used this measure as a continuous meta-regressor in our moderator analyses.

ORs and their corresponding confidence intervals were complemented by prediction intervals. Prediction intervals estimate the range of effects that are to be expected from new studies sampled at random from the same population taking both effect size variation and between-study heterogeneity into account (Spineli & Pandis, 2020). We also assessed if individual studies had large impact on the meta-analyses due to high weights or being outliers. Finally, we computed impact sensitivity analyses by systematically omitting individual studies from the analyses using leave-one-out analyses.

According to the PRISMA 2020 guidelines (Page et al., 2021), a risk of bias assessment is required for systematic reviews and meta-analyses. Therefore, in order to assess risk of bias, we assessed small study bias through Egger's *t* test and funnel plot asymmetry (Egger et al., 1997). We also assessed publication bias using a Bayesian approach through the RoBMA function that averages across selection models as well as precision-effect test and precision-effect estimate with standard errors (PET-PEESE) models to provide a complementary measure of publication bias beyond small study bias. Further risk of bias assessment was deemed unnecessary as bias is more relevant to meta-analyses of clinical studies that, for example, assess whether studies were randomized-controlled trials or double-blinded. Since we assessed hand preference which was often not at the core of the research question of the individual studies, we do not believe that any bias assessments beyond small study and publication bias are critical. Furthermore, since all but one of the included studies are published and have been reviewed by peers, the large majority of studies was subjected to a rigorous review process likely resulting in sufficient study quality overall. Finally, the inclusion of case-control studies only ensures that all procedures that can strongly influence the base rate of hand preference were matched between the individuals with dyslexia and healthy controls and thus cannot account for any effects in the data.

For visualization, we used forest plots to depict the individual study ORs as well as the overall effect estimate. Please note that forest plots of individual studies use the log OR instead of the OR because visualization of large confidence intervals is difficult otherwise. Log ORs center around 0 instead of 1 for a null effect and range from minus to plus infinity instead of from 0 to plus infinity. Thus, log ORs center symmetrically around 0.

**Results**

Descriptive data including hand preference distribution as well as moderators for all 68 studies that met all inclusion criteria as well as the 14 exploratorily included studies with a missing IQ criterion are presented in Table 1. The exploratory studies were solely included to assess their influence on the observed result pattern and were not included for assessments of between-study heterogeneity or publication bias.

*Meta-analysis on non-right-hand preference*

Overall, $k$ = 68 studies totaling $n$ = 4660 individuals with dyslexia and $n$ = 40845 controls were included in the meta-analysis on non-right-hand preference. The OR between individuals with dyslexia and controls reached significance (OR = 1.37, CI = [1.14; 1.65], $z$ = 3.32, $p$ < .001) suggesting higher rates of non-right-hand preference in individuals with dyslexia (Figure 2). Leave-one-out analyses confirmed that this effect was not due to individual outliers as leaving out any study still resulted in a significant difference (see Figure 3). The fact that the prediction interval includes the OR value of 1.0 (0.59 to 3.20) does not allow for a high degree of certainty about the results of this analysis. Robust Bayesian meta-analysis revealed strong evidence for an effect ($BF_{10}$ = 25.57). Using wider priors resulted in evidence in favor of the alternative hypothesis as well (see Supplementary Table 1).

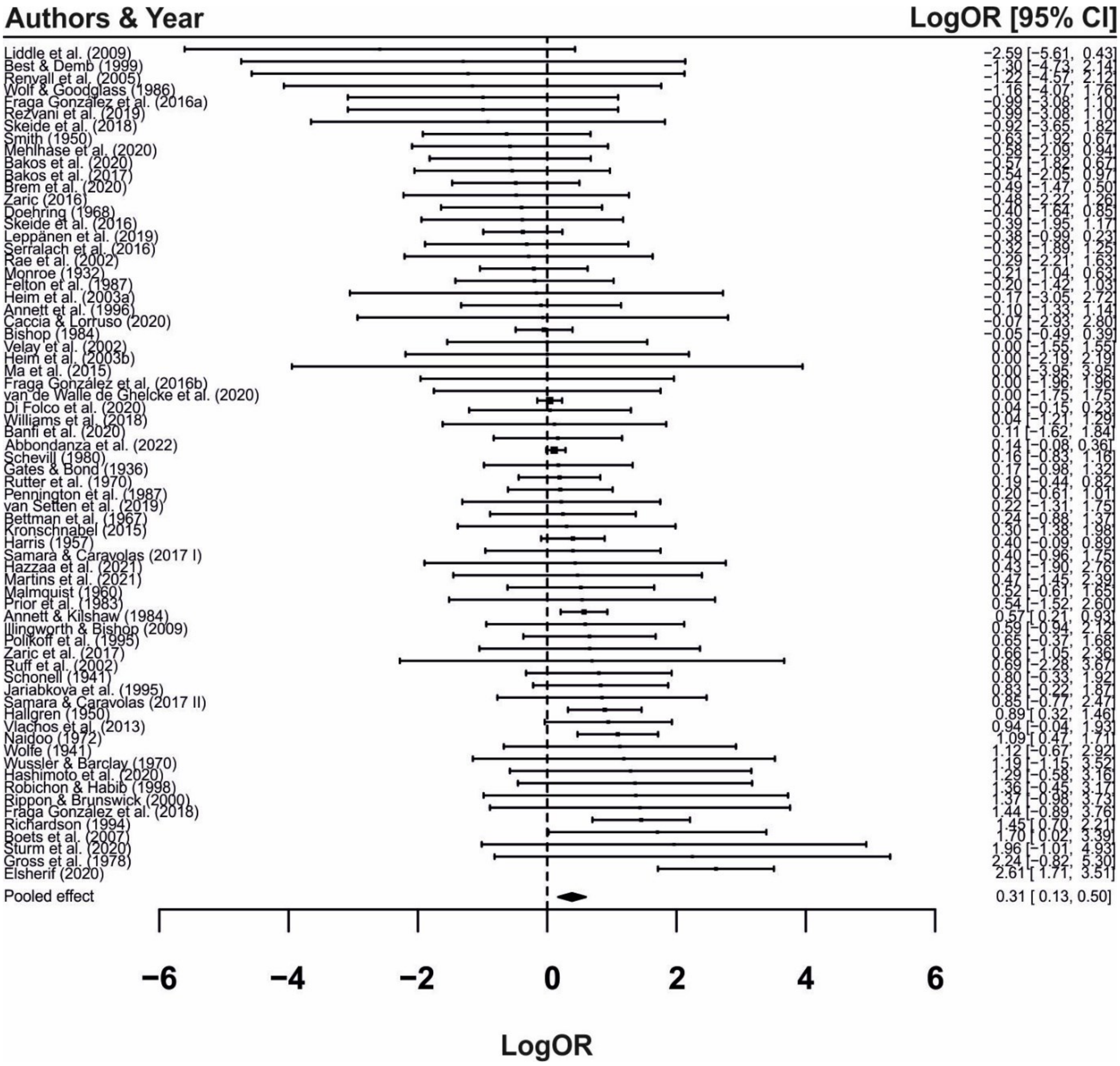


*Figure 2. Forest plot of non-right-hand preference Odds Ratios (ORs) between individuals with dyslexia and controls for each individual study. The pooled effect is indicated as a diamond at the bottom. The width of the diamond indicates the 95% CI of the pooled effect. Note that ORs were log-transformed for illustration. Thus, a value of 0 indicates no difference between individuals with dyslexia and controls with respect to non-right-hand preference. Positive values indicate higher rates of non-right-hand preference in individuals with dyslexia compared to controls whereas negative values indicate higher rates of non-right-hand preference in controls compared to individuals with dyslexia.*

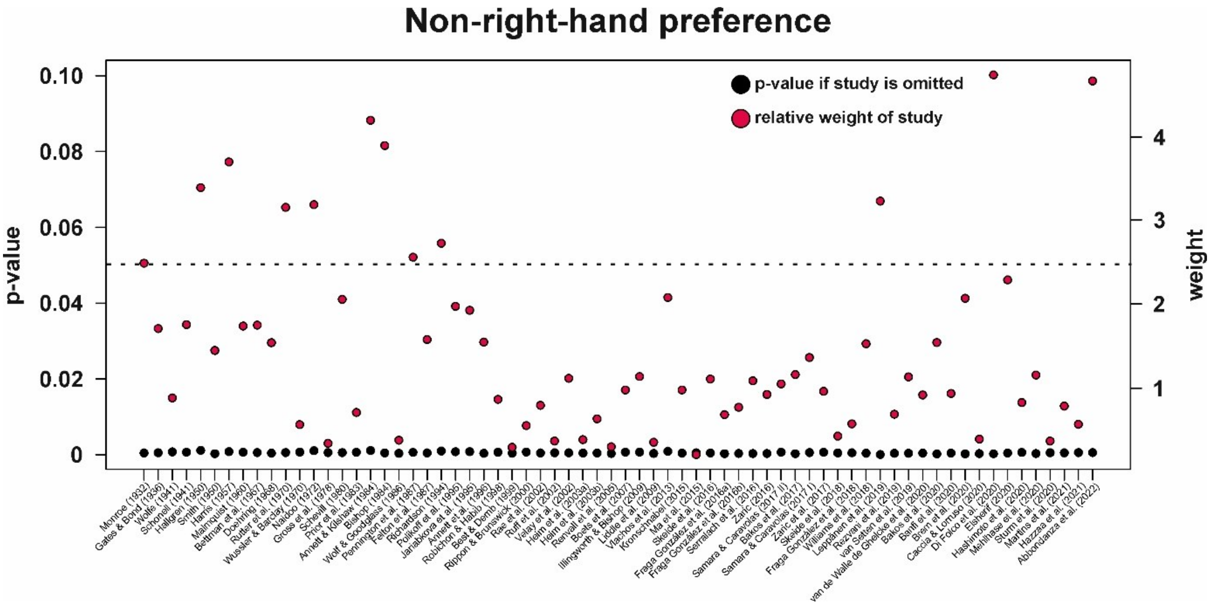


*Figure 3. Leave-one-out results and weight analysis for the meta-analysis on non-right-hand preference. Black dots represent the significance level of the meta-analysis in case the listed study is omitted. Red dots indicate the relative weight of the listed study in the meta-analysis. The dashed line represents the alpha level of p = .05. Studies are ordered by publication year.*

An assessment for heterogeneity revealed strong evidence supporting the presence of between-study variability ($Q_{(67)} = 103.69$, $p < .001$, $BF_{10} > 100$, $I^2 = 48.27\%$, $\tau^2 = 0.18$), hence we conducted further moderator analyses to identify potential sources of between-study heterogeneity. We found no significant influences of publication year, hand preference assessment, hand preference classification system, sex ratio, ancestry, diagnostic method, or IQ cut-off (all *p*s > .116). We did, however, find a significant moderating effect of age ($Q_{(1)} = 14.99$, $p < .001$) that suggests a positive association between the mean age and the resulting ORs between individuals with dyslexia and controls ($b = 0.13$, CI = [0.06; 0.19], $p < .001$, Figure 4). Mean ages in the included studies ranged from 5.46 to 25.40 years. An assessment of small study bias showed no funnel plot asymmetry ($z = -0.80$, $p = .421$, Supplementary Figure 1). There was additionally strong evidence against the presence of publication bias ($BF_{10} = 0.09$).

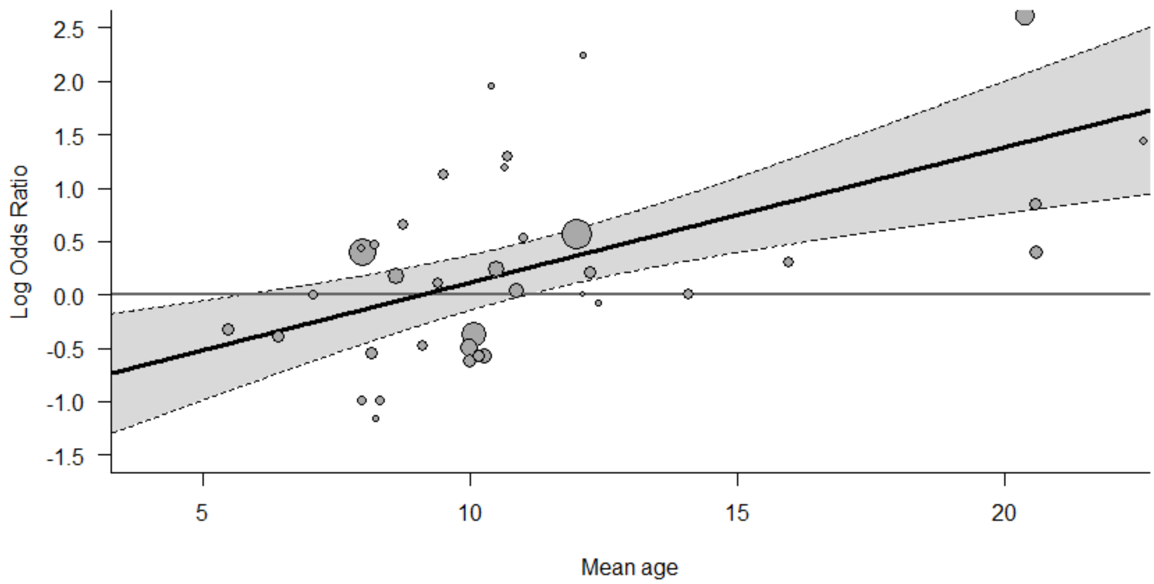


*Figure 4. Odds ratios (ORs) of non-right-hand preference between individuals with dyslexia and controls as a function of mean age of the sample. ORs significantly increased with age. For illustration, ORs were log-transformed. An OR value of 0 indicates no difference between individuals with dyslexia and controls with respect to the prevalence of non-right-hand preference.*

We repeated the analysis including $k = 13$ additional studies without a clear IQ cut-off comprising a total of $n = 5525$ individuals with dyslexia and $n = 42112$ controls. While Stella (2018) also had an unclear IQ cut-off criterion, this study was not included in this analysis as it used a Non-left-Left classification system. The findings remained largely unchanged (OR = 1.38, CI = [1.17; 1.62], $z = 3.82$, $p < .001$, PI = [0.63; 3.01], $BF_{10} = 41.38$) suggesting that these studies followed the observed result pattern. A forest plot including the added studies can be found in the supplements (Supplementary Figure 2).

*Meta-analysis on left-hand preference*

Overall, $k = 61$ studies totaling $n = 2702$ individuals with dyslexia and $n = 14385$ controls were included in the meta-analysis on left-hand preference. The OR between individuals with dyslexia and controls reached significance (OR = 1.25, CI = [1.02; 1.50], $z = 2.22$, $p = .013$) suggesting higher rates of left-hand preference in individuals with dyslexia (Figure 5). Leave-one-out analyses indicated that the analysis remained significant irrespective of which study was excluded from the analysis (Figure 6). The prediction interval ranged from values below and above 1.0 (PI = 0.70; 2.26) indicating uncertainty if newly sampled studies would also support the hypothesis of higher rates of left-hand preference in individuals with dyslexia. Robust Bayesian meta-analysis suggested anecdotal to moderate evidence in favor of the alternative hypothesis ($BF_{10}$ = 2.46). Using wider priors resulted in evidence in favor of the alternative hypothesis as well, albeit to a smaller extent (see Supplementary Table 1). For a prior scale of 0.707, there was only anecdotal evidence for an effect ($BF_{10}$ = 1.19).

An assessment for heterogeneity did not reach significance ($Q_{(60)} = 57.81$, $p = .556$, $I^2 = 14.56\%$, $\tau^2 = 0.08$). While the corresponding Bayes factor indicated that there was anecdotal evidence in favor of heterogeneity, the evidence was negligible ($BF_{10}$ = 1.60). We thus decided against further moderator analysis. An assessment of small study bias showed no funnel plot asymmetry ($z = 0.06$, $p = .949$, Supplementary Figure 3) as well as moderate evidence against the presence of publication bias ($BF_{10}$ = 0.29).

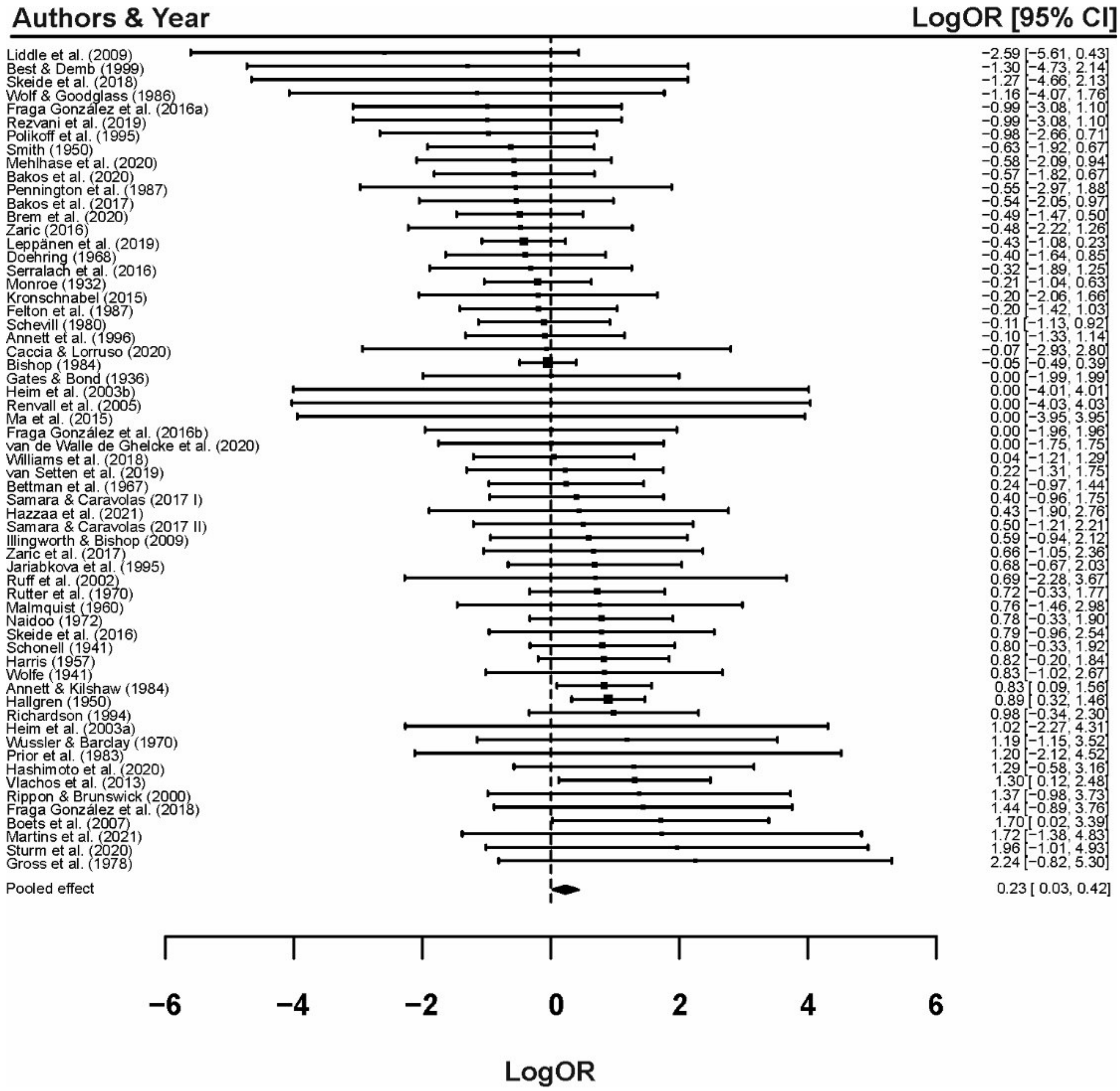


*Figure 5. Forest plot of left-hand preference Odds Ratios (ORs) between individuals with dyslexia and controls for each individual study. The pooled effect is indicated as a diamond at the bottom. The width of the diamond indicates the 95% CI of the pooled effect. Note that ORs were log-transformed for illustration. Thus, a value of 0 indicates no difference between individuals with dyslexia and controls with respect to left-hand preference. Positive values indicate higher rates of left-hand preference in individuals with dyslexia compared to controls whereas negative values indicate higher rates of left hand-preference in controls compared to individuals with dyslexia.*

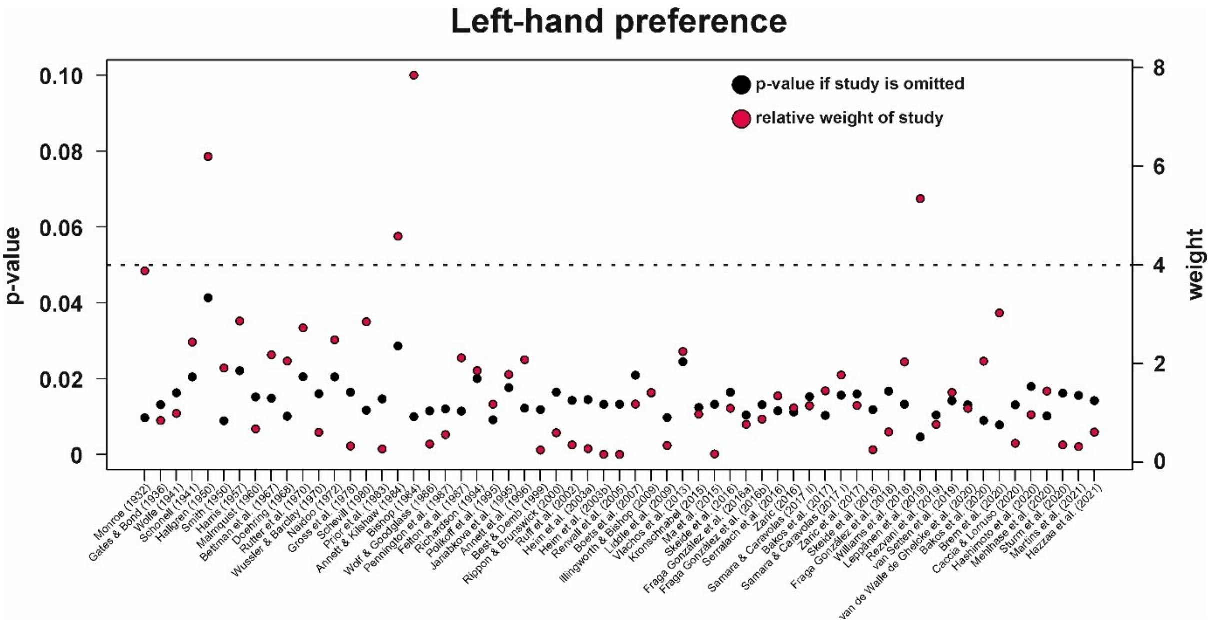


*Figure 6. Leave-one-out results and weight analysis for the meta-analysis on left-hand preference. Black dots represent the significance level of the meta-analysis in case the listed study is omitted. Red dots indicate the relative weight of the listed study in the meta-analysis. The dashed line represents the alpha level of p = .05. Studies are ordered by publication year.*

We repeated the analysis including $k = 11$ additional studies that did not have a clear IQ cut-off comprising a total of $n = 3504$ individuals with dyslexia and $n = 19145$ controls. The findings remained largely unchanged (OR = 1.22, CI = [1.02; 1.44], $z = 2.23$, $p = .013$, PI = [0.74; 2.00], $BF_{10} = 1.61$), again suggesting that these studies did not have a strong influence on the overall result pattern. A forest plot including the added studies can be found in the supplements (Supplementary Figure 4).

*Meta-analysis on mixed-hand preference*

Overall, $k = 24$ studies totaling $n = 1199$ individuals with dyslexia and $n = 3193$ controls were included in the meta-analysis on mixed-hand preference. The OR between individuals with dyslexia and controls reached significance (OR = 1.55, CI = [1.23; 1.96], $z = 3.69$, $p < .001$) suggesting higher rates of mixed-hand preference in individuals with dyslexia (Figure 7).

Leave-one-out analyses suggested that this finding was unaffected by individual influential studies or outliers as leaving out any studies still resulted in a significant effect (see Figure 8). The prediction interval suggested that if new studies were to be sampled, they would likely find an OR above 1.0 (PI = 1.07; 2.26) suggesting a good level of certainty in the results. Robust Bayesian meta-analysis indicated strong evidence in favor of the alternative hypothesis ($BF_{10}$ = 22.70) further supporting the notion that rates of mixed-hand preference are higher in individuals with dyslexics compared to controls. Using wider priors resulted in strong evidence in favor of the alternative hypothesis as well (see Supplementary Table 1).

An assessment for heterogeneity did not reach significance ($Q_{(23)} = 19.62$, $p = .665$, $I^2 = 6.68\%$, $\tau^2 = 0.02$). The corresponding Bayes factor suggested anecdotal evidence against the presence of heterogeneity ($BF_{10}$ = 0.73). We thus decided against further moderator analysis. An assessment of small study bias showed no funnel plot asymmetry ($z = -0.59$, $p = .552$, Supplementary Figure 5) as well as moderate evidence against the presence of publication bias ($BF_{10}$ = 0.32).

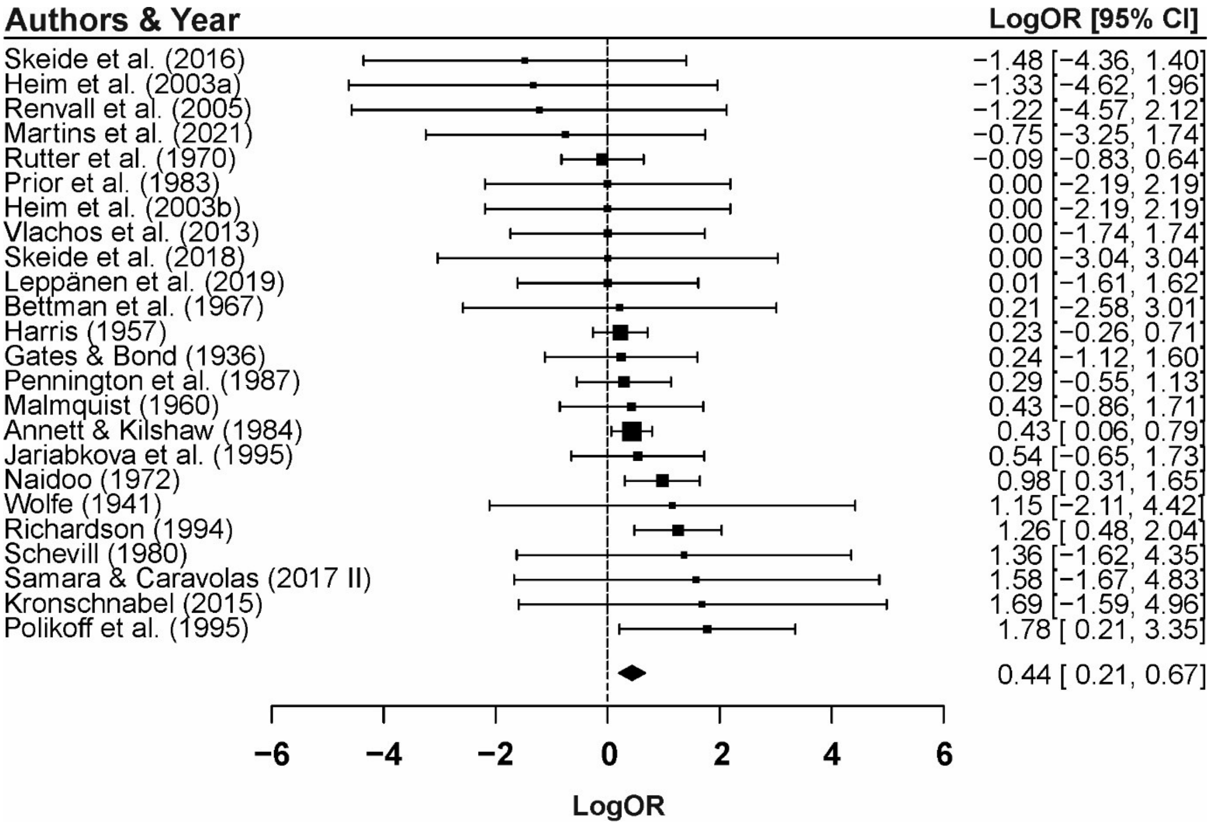


*Figure 7. Forest plot of mixed-hand preference Odds Ratios (ORs) between individuals with dyslexia and controls for each individual study. The pooled effect is indicated as a diamond at the bottom. The width of the diamond indicates the 95% CI of the pooled effect. Note that ORs were log-transformed for illustration. Thus, a value of 0 indicates no difference between individuals with dyslexia and controls with respect to mixed-hand preference. Positive values indicate higher rates of mixed-hand preference in individuals with dyslexia compared to controls whereas negative values indicate higher rates of mixed hand-preference in controls compared to individuals with dyslexia.*

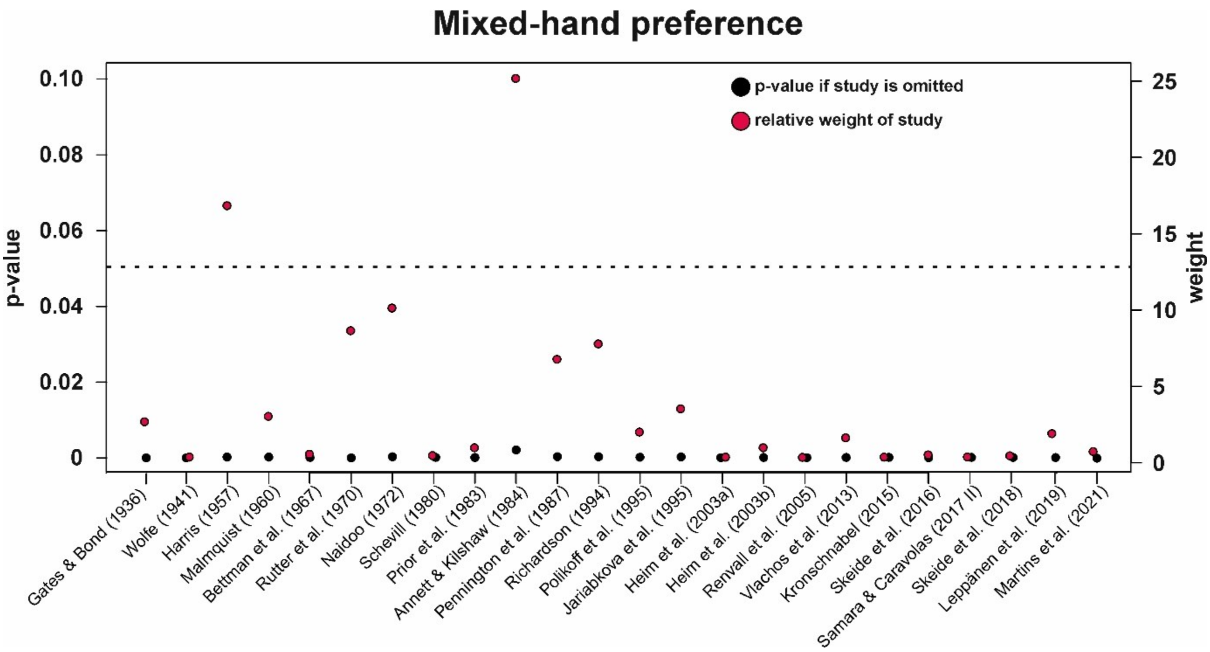


*Figure 8. Leave-one-out results and weight analysis for the meta-analysis on mixed-hand preference. Black dots represent the significance level of the meta-analysis in case the listed study is omitted. Red dots indicate the relative weight of the listed study in the meta-analysis. The dashed line represents the alpha level of p = .05. Studies are ordered by publication year.*

To explore the effect of including the studies without a clear IQ cut-off, $k = 4$ additional studies comprising a total of $n = 1382$ individuals with dyslexia and $n = 3630$ controls were added to the analysis. The findings again complemented the results without including these studies as the findings were more robust and did not change the overall result pattern (OR = 1.57, CI = [1.26; 1.95], $z = 4.04$, $p < .001$, PI = [1.15; 2.13], $BF_{10} = 34.11$). A forest plot including the added studies can be found in Supplementary Figure 6.

## Discussion

To answer the question of whether handedness differences (assessed as hand preference) are to be found between individuals with dyslexia and typically developing individuals, three separate sets of meta-analyses were conducted. Meta-analysis 1 (non-right-hand preference) included $k = 68$ studies totaling $n = 4660$ individuals with dyslexia and $n = 40845$ controls in the analysis. Meta-analysis 2 (left-hand preference) included $k = 61$ studies totaling $n = 2702$ individuals with dyslexia and $n = 14385$ controls. Meta-analysis 3 (mixed-hand preference) included $k = 24$ studies totaling $n = 1199$ individuals with dyslexia and $n = 3193$ controls. Therefore, the present study had a substantially larger sample size than the previous attempts to integrate data on dyslexia and hand preference by Bishop (1990) and Englinton and Annett (1994) both of which included $k = 25$ studies. It can therefore be assumed that the present findings are not only up-to-date, but also substantially more robust than the previous studies' findings.

The meta-analysis on non-right-hand preference revealed a significant effect with an OR of 1.37, indicated higher rates of non-right-hand preference in individuals with dyslexia. This translates to a percentage of 23.24% individuals with dyslexia being non-right-handed (with the corresponding percentage in the general population being 18.1%; (Papadatou-Pastou et al., 2020)). Both leave-one-out analysis and Bayesian statistics confirmed this effect. Also, the addition of studies without clear IQ cut-off to the sample did not change the results meaningfully. Heterogeneity was high, suggesting an influence of moderator effects. While publication year, hand preference assessment, hand preference classification system, sex ratio, ancestry, diagnostic method, or IQ cut-off did not seem to have an influence, the mean age of the investigated cohorts did affect the results. Specifically, there were larger ORs if cohorts were older on average, potentially suggesting a role of developmental effects (Michel et al., 2018; Nelson et al., 2014) for the association between non-right-hand preference and dyslexia. While developmental effects are certainly a possibility, it needs to be noted that none of the included studies used longitudinal designs. Since findings from cross-sectional studies could be confounded by cohort effects other than age across the different studies, future longitudinal research is needed. Publication bias did not seem to have affected the results of this meta-analysis. Of note, the prediction interval for this analysis includes the odds ratio value of 1.0 (0.59 to 3.20), therefore caution is needed when interpreting the results of this analysis. This wide interval casts doubt as to whether newly sampled studies would also support the hypothesis of higher rates of non-right-hand preference in individuals with dyslexia.

The meta-analysis on left-hand preference revealed a significant effect with an OR of 1.25, indicated higher rates of left-hand preference in individuals with dyslexia. This translates to a percentage of 12.91% individuals with dyslexia being left- handed (with the corresponding percentage in the general population being 10.6%; Papadatou-Pastou et al., 2020). While leave-one-out analyses confirmed that this effect was not driven by individual studies, the Bayesian analysis did not reach the threshold of moderate evidence using a small effect prior. If wider priors were used, there was only anecdotal evidence supporting the alternative hypothesis indicating that we need more research to determine whether there are increased rates of left-hand preference in individuals with dyslexia. The addition of studies without clear IQ cut-off to the sample did not change the results meaningfully. Unlike the first meta-analysis, no significant heterogeneity was detected. Again, publication bias did not seem to have affected the results of this meta-analysis. Similarly to the non-right-hand preference meta-analysis, the prediction interval for the left-hand preference meta-analysis includes the value of 1.0 (PI = 0.70; 2.26) not allowing for a high degree of certainty about the results of this analysis.

The meta-analysis on mixed-hand preference revealed an OR of 1.55, indicated higher rates of mixed-hand preference in individuals with dyslexia. This translates to a percentage of 11.23% individuals with dyslexia being mixed-handed (with the corresponding percentage in the general population being 9.33%; (Papadatou-Pastou et al., 2020)). The leave-one-out analysis confirmed this effect. Also, the addition of studies without clear IQ cut-off to the sample did not change the results meaningfully. Unlike the first meta-analysis, no significant heterogeneity was detected. Publication bias did not seem to have affected the results of this meta-analysis. Contrasting left- and non-right-hand preference, the prediction interval for the analysis of mixed-hand preference did not include 1.0 (PI = 1.07; 2.26) allowing a good level of certainty in the finding of increased levels of mixed-hand preference in individuals with dyslexia compared to controls. Moreover, the Bayesian statistics indicate strong evidence in favor of the alternative hypothesis ($BF_{10}$ = 22.70) that was robust across priors.

Taken together, the present findings suggest that individuals with dyslexia show elevated levels of atypical hand preference (non-right-, left-, and mixed-hand preference) compared to controls. However, since our findings for left-hand preference were not robustly favoring evidence in favor of an effect using a robust Bayesian approach, it seems likely that the effects in the non-right-hand preference meta-analysis were largely due to elevated levels of mixed-hand preference in individuals with dyslexia. The meta-analysis on mixed-hand preference showed high robustness, the highest OR as well as high certainty in future effects, but our conclusions might be limited to children and young adults due to the limited range of age groups in our primary studies. Therefore, it can be hypothesized that the underlying mechanisms involved in the development of dyslexia may share similarities with the mechanisms underlying handedness strength, but not handedness direction. In fact, degree of handedness may be a more suitable indicator of cerebral organization and behavior than the direction of handedness. Previous research has indeed indicated cognitive differences between individuals with weak and strong hand preference (Prichard et al., 2013) or inconsistent and consistent handedness (Christman & Prichard, 2016) as weak hand preference or inconsistent hand use across tasks has been associated with better episodic memory recall as well as higher cognitive flexibility. Moreover, comparisons between individuals with strong and weak hand preference, regardless of the direction of asymmetry, have revealed significant behavioral differences in both humans and nonhuman species (Hardie & Wright, 2014; Rogers, 2017). The differentiation between handedness direction and degree is also important on a neurobiological level because these two aspects seem to be independently encoded in the brain (Dassonville et al., 1997). Additionally, variations in the degree of handedness have been associated with differences in structural lateralization in somatomotor regions of the brain and areas related to high-level cognitive control of action (McDowell et al., 2016). Furthermore, specific genetic polymorphisms in the *PCSK6* gene have been linked to the degree of handedness, rather than the direction of handedness (Arning et al., 2013).

While our results generally indicate that degree of handedness rather than direction seems to be critical in dyslexia, conclusions drawn from this study must be treated with caution as information about degrees of handedness generally requires the assessment of continuous measures such as lateralization quotients. Unfortunately, as the large majority of studies did not provide continuous scores of handedness for their participants, we were unable to analyze this question in further detail which limits the conclusions about possible distinctions between direction and degree of handedness within the present study. This goes hand in hand with the observation that only a small subset of studies used dedicated handedness inventories that allow for the quantification of lateralization quotients. We hope that future research will tackle this question by regularly applying handedness inventories and report their results to more thoroughly understand the association between handedness and dyslexia.

One further limitation of the present study is that definitions of mixed-hand preference were highly diverse across studies due to differing criteria how to define mixed-hand preference. A recent study has highlighted this issue in the literature as these terms leave ambiguity as to what is actually being measured (Vingerhoets et al., 2023). In total, $k$ = 13 of 28 studies eligible for the mixed-hand preference meta-analysis claimed that they measured ambidexterity, meaning that individuals were equally skilled with both hands within one task, whereas $k$ = 5 studies reported mixed-handedness to reflect inconsistent hand preferences within an individual for different tasks. The rest of the studies did not provide any information what their reported mixed-hand preferences reflect. Interestingly, even though studies claimed to measure ambidexterity, the criterion that was reported in some of these studies actually referred to a lateralization quotient that is usually measured across tasks such as in the EHI (Oldfield, 1971). While lateralization quotients of -100 or +100 clearly indicate consistent left- or right-hand preferences, lateralization quotient of 0 can be indicative of both ambidexterity as well as inconsistent hand use. Thus, labels of ambidexterity or inconsistent hand use need to be treated with caution unless the study is explicit about how mixed-hand preferences were measured. Given this limitation of our study, it will be critical for future studies to disambiguate if the association we found for mixed-hand preference and dyslexia is primarily related to inconsistent handedness, ambidexterity or both phenotypes. We furthermore urge researchers in this domain to carefully report how their categories of hand preferences were computed and what criteria they used to assess ambidexterity or inconsistent hand preferences across tasks.

Recent genome-wide association studies (GWAS) studies in large samples demonstrate that handedness has a complex polygenic nature (Cuellar-Partida et al., 2020). Some of the involved genes have also been implicated in neurodevelopmental conditions, including schizophrenia and dyslexia (Brandler et al., 2013; Brandler & Paracchini, 2014; Cuellar-Partida et al., 2020; Wiberg et al., 2019). Thus, an important question is to ask whether associations between handedness and brain asymmetries could be mediated by shared genetics. In a recent study, Sha and colleagues (Sha et al., 2021) assessed the relationship between handedness and cortical asymmetries by generating asymmetry maps for cortical thickness and surface area in 28,802 right-handed and 3062 left-handed UK Biobank participants. They found several regions that differed between left- and right-handers, consistent with a shift of neuronal resources to the hemisphere controlling the dominant hand. This means a general less leftward/more rightward shift for left-handers, who have a right hemisphere dominance for the preferred hand. Next, the same study derived polygenic risk scores (PRS) for left-handedness in an independent training sample of individuals from the UK Biobank to be tested in the target sample of individuals selected for the initial brain imaging analysis. As expected, the PRS were associated with left-handedness in the target sample. However, the handedness PRS also showed associations with cortical surface area asymmetries that differed between left- and right-handers. Specifically, PRS increasing the chances of left-handedness were associated with increased average rightward asymmetry in the fusiform cluster and decreased average leftward asymmetry in the anterior insula clusters. Tubulin-associated genes featured among the genes associated with cortical asymmetries. This is not surprising considering that these types of genes were enriched in the associations with handedness.

Studies included in the present meta-analyses used for the most part hand preference measures, such as the Edinburgh Handedness Inventory (but also note that a number of studies did not report the way they measured handedness). However, hand preference and hand skill are different manifestations of handedness, that correlate only to a medium degree (0.46 between the Edinburgh Handedness Inventory and the pegboard task (Mundorf et al., 2023)), although it has been stressed that the correlation between hand preference and hand skill is dependent on which test is used to assess hand skill (Buenaventura Castillo et al., 2020). What is more, there is evidence that hand skill might be more sensitive in detecting possible relationships between handedness and cognitive ability. For instance, one study reported a negligible association between hand preference and cognitive ability, yet did report an association between cognitive ability and hand skill, with moderate right-handers having higher ability scores compared to strong left- and strong right-handers (Nicholls et al., 2010). Crow and colleagues (Crow et al., 1998) further showed cognitive deficits close to the point of equal hand skill using data from the National Child Development Study. Moreover, Brandler and colleagues (Brandler et al., 2013) detected candidate genes statistically associated with handedness, when handedness was measured as hand skill. Thus, for future empirical studies on dyslexia and handedness it would be important to assess both phenotypes to investigate an effect of handedness assessment method.

For future meta-analyses, it would also be important to conduct comparisons not only between individuals with dyslexia and controls, but also to group individuals with dyslexia into those who have phonological deficits and those who do not (Illingworth & Bishop, 2009; Leonard & Eckert, 2008). For example, it has been shown in one small-sample study that individuals with dyslexia with phonological deficits had a higher rate of left-handedness (29.4%) than individuals with dyslexia without phonological deficits (0%) (Annett et al., 1996). Moreover, a dichotic listening study in individuals with dyslexia has also shown that dyslexia subtypes matter for laterality research, with individuals with dyslexia with strong symptoms showing a reduction of the typical right ear-advantage in the dichotic listening task, while individuals with dyslexia with weak symptoms did not (Helland et al., 2008). Unfortunately, a subgroup analysis was not possible in the present study due to a lack of suitable studies. Future empirical studies on the association between dyslexia and handedness should therefore include dyslexia subtypes to allow for such analyses in the future.

Another comparison that future meta-analyses should consider is between the different criteria to diagnose dyslexia, especially with respect to IQ. Di Folco and colleagues (Di Folco et al., 2022) recently reported a higher frequency of non-right-handedness in dyslexia based on DSM-5 (OR = 1.24, $p$ = .003) that is comparable to our findings. However, when applying the ICD-11 criteria which are based on reading-IQ discrepancy, the effect disappeared. Di Folco and colleagues (Di Folco et al., 2022) suggest that the original effect is not specific to reading but is mediated by IQ. In fact, they found that the prevalence of non-right-handedness does not differ between individuals with dyslexia and controls, once sex and IQ are controlled for. This comparison was unfortunately not possible within our dataset, as most studies only reported IQ cut-offs and did not provide numerical information, i.e. IQ scores for individuals with dyslexia and controls, on this issue for further analysis.

A number of moderators (e.g., sex) were not investigated within this meta-analysis, as the original studies did provide data at different levels of the variables. In other cases, not all studies reported the necessary data for analysis. We would thus like to strongly support previously voiced recommendations for adopting good practices (Papadatou-Pastou et al., 2020), such as uploading raw data sets in open-access repositories (e.g., the Open Science Framework), making them available for meta-analysts. Ideally, the data sets should include detailed information about participant characteristics (e.g., sex, age, ancestry), the measurement of handedness (including both hand skill and hand preference measurements) and the measurement of dyslexia (including how IQ was assessed).

Our findings do not allow us to provide concrete recommendations for educators and clinicians, as the relationship between hand preference and dyslexia was found to be robust only for mixed-hand preference. However, as discussed earlier, mixed-handedness, as operationalized in the context of the present meta-analysis, lacked a clear and consistent definition, essentially representing a third, 'middle' category assessed using varying criteria. Therefore, further research is necessary before any conclusions can be drawn regarding whether mixed-hand preference could serve as a biomarker for dyslexia. Moreover, the absolute percentage of individuals with dyslexia who are mixed-handed was found to be 11.23%, when this percentage in the general population is 9.33% (Papadatou-Pastou et al., 2020). Consequently, even if the association between mixed-handedness and dyslexia is confirmed by future studies, it may not have strong diagnostic value.

Overall, we report three meta-analyses of all available studies on the relationship between hand preference and dyslexia. Evidence of a link between hand preference and dyslexia, albeit inconclusive, was found for the non-right-hand preference and the left-hand preference comparisons. Robust evidence was found for the mixed-hand preference comparison. These relationships correspond to absolute percentages of 23.24%, 12.91%, and 11.23% for non-right-, left- and mixed-hand preference in dyslexia (18.1%, 10.6%, and 9.33% for the general population respectively). Therefore, the evidence for a relationship between dyslexia and hand preference is strong, but the absolute difference in atypical hand preference between individuals with dyslexia and controls is rather small. Our findings align with the emerging genetic research that indicates the involvement of shared genes and biological pathways in lateralization and dyslexia.

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**Data availability statement**

All data and code for analysis are available under the following link: https://osf.io/waqj4/?view_only=c21a6f7342fd47f8b1eb572945e31c50.

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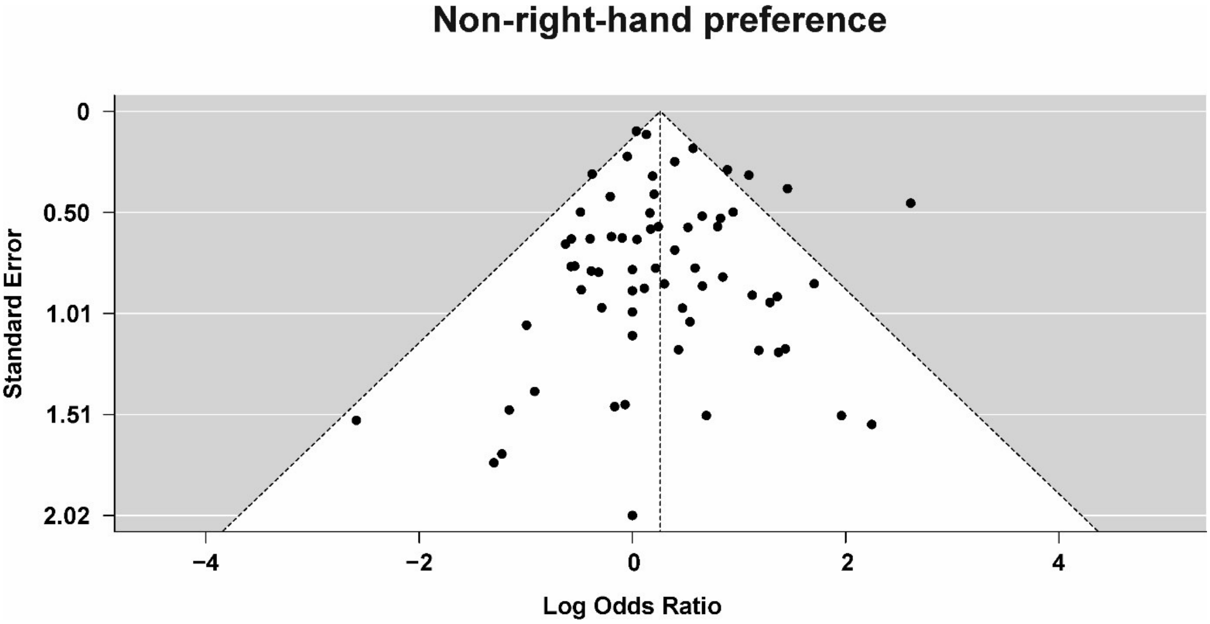
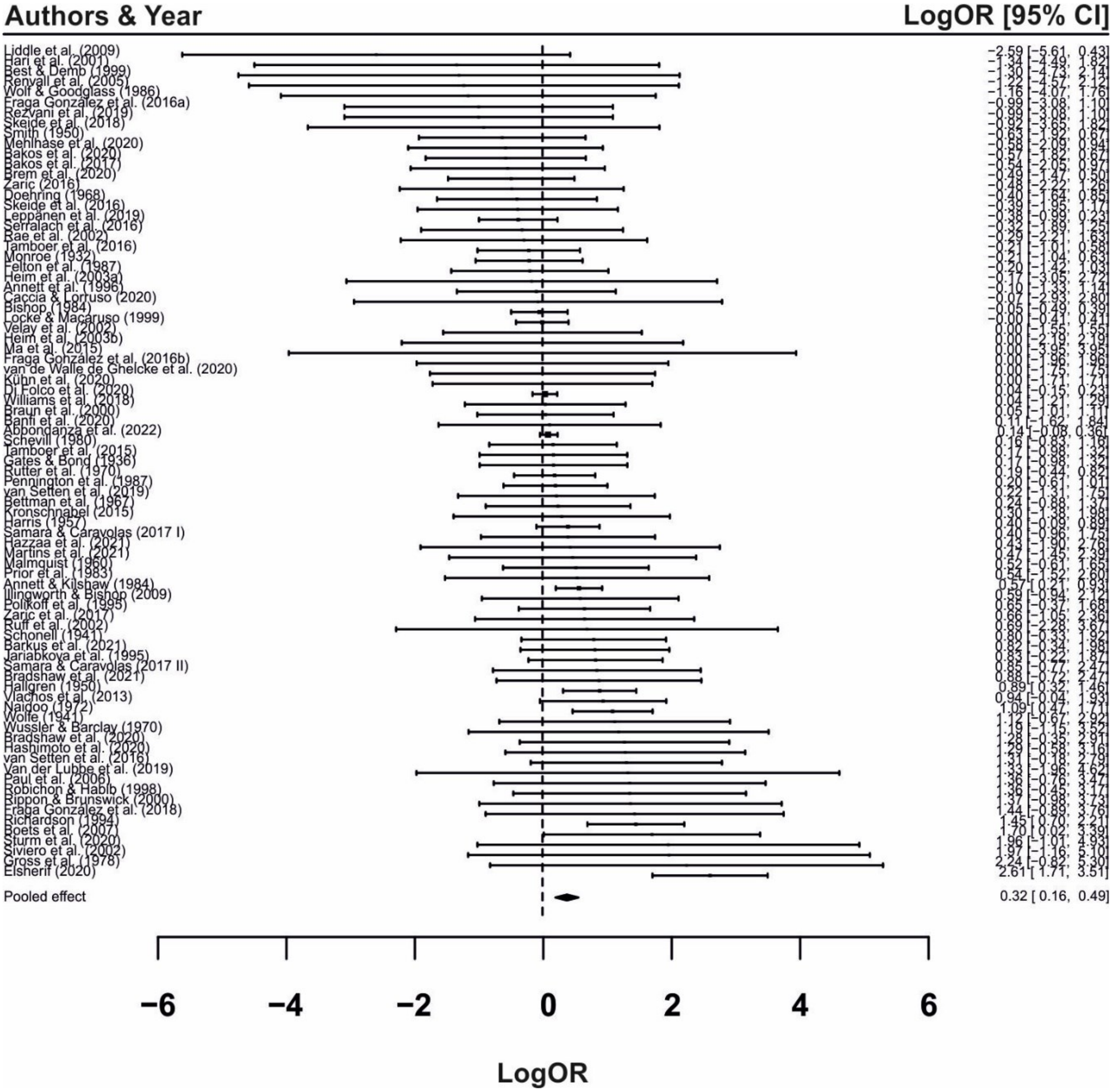
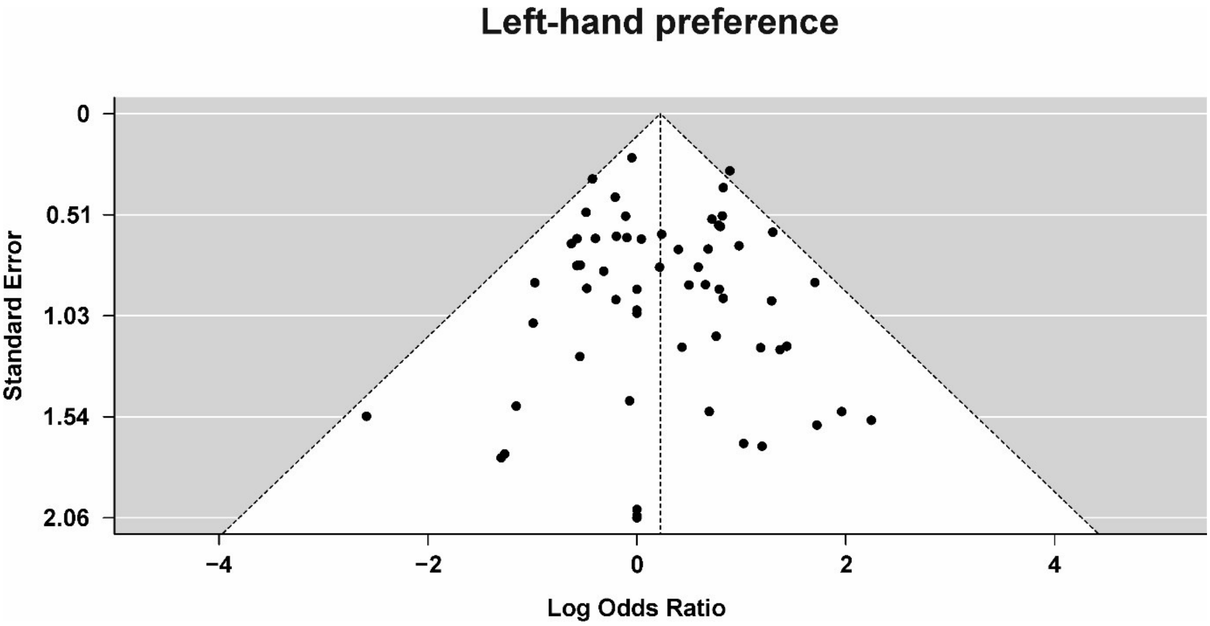
**Supplementary materials**



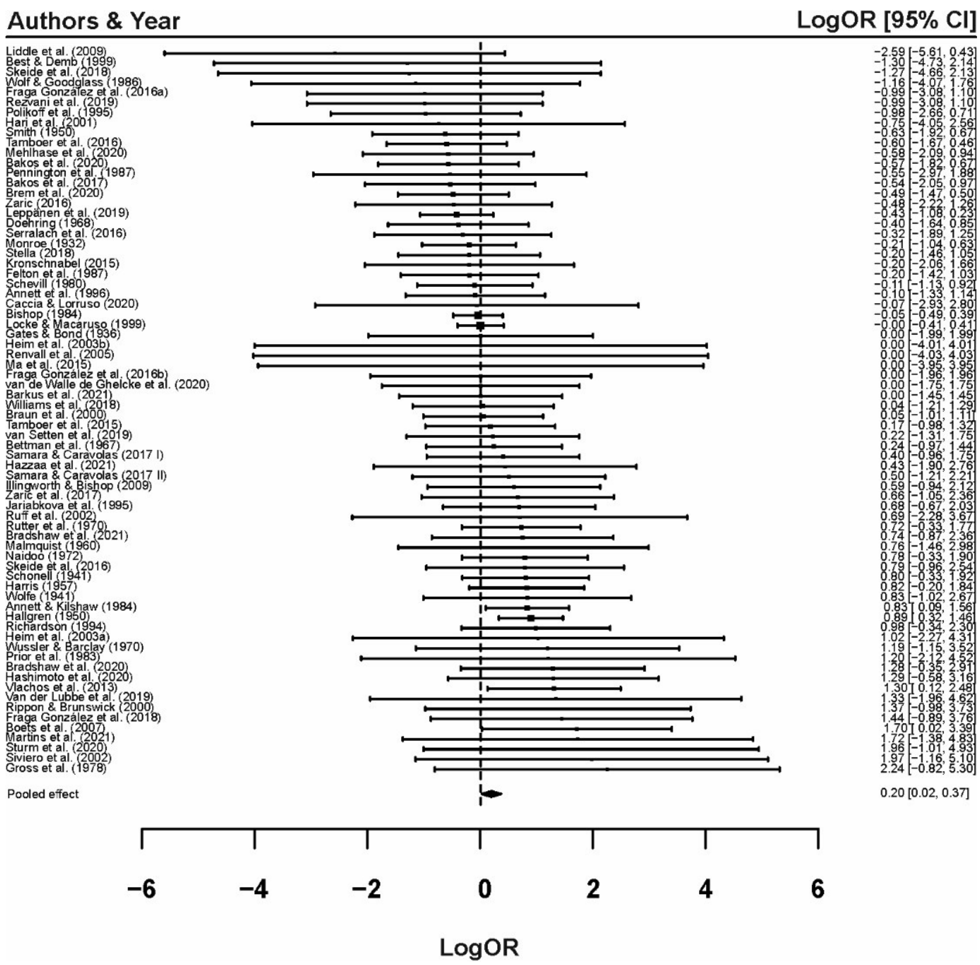

*Supplementary Figure 1. Funnel plot for non-right handedness. No asymmetry in the funnel plot could be detected.*



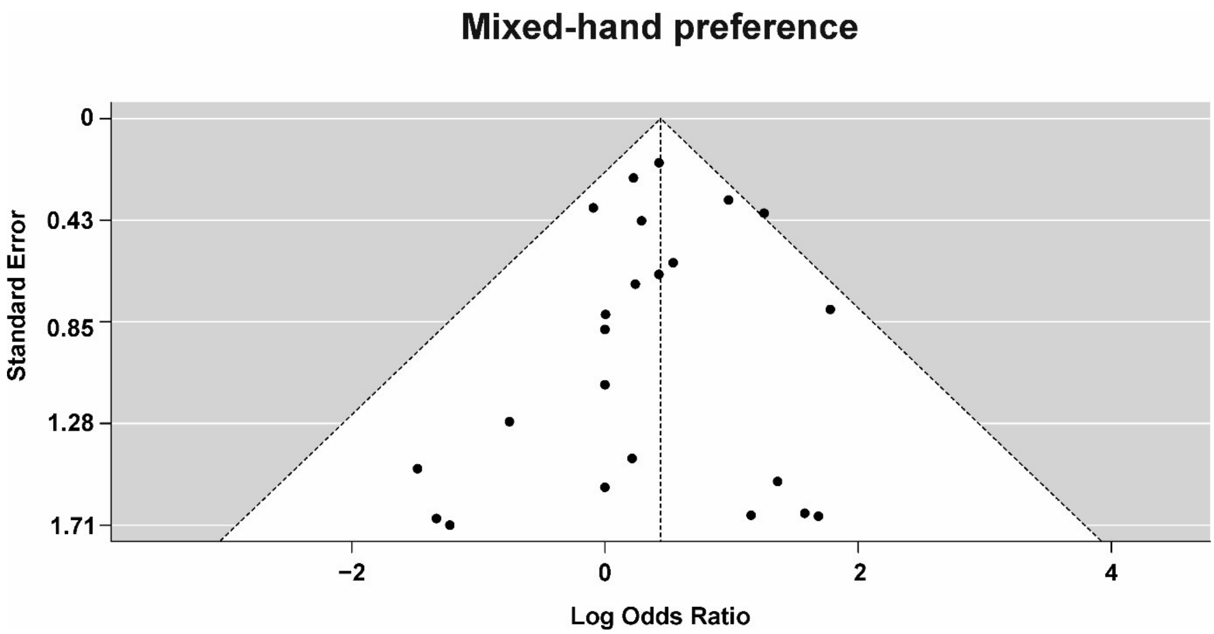

*Supplementary Figure 2. Forest plot for non-right-handedness including the studies that did not have a clear IQ criterion.*



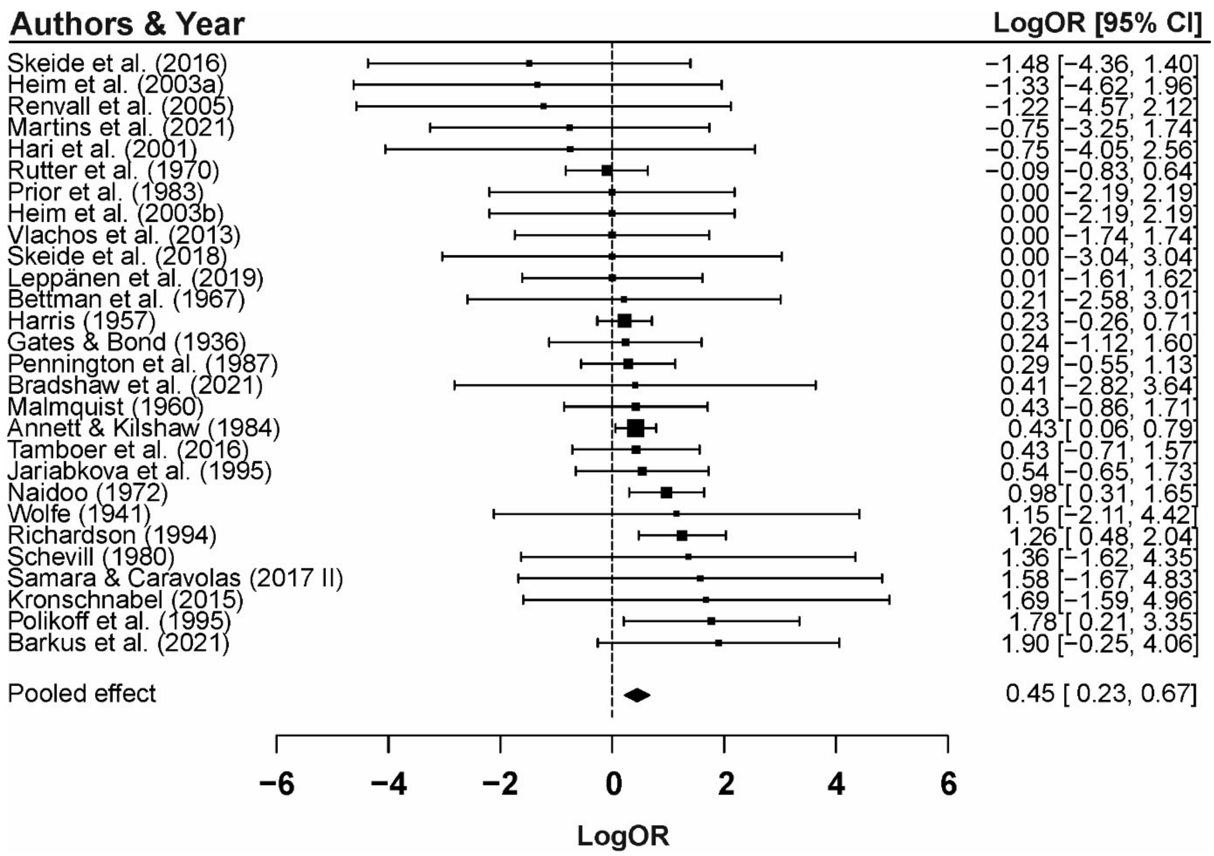

*Supplementary Figure 3. Funnel plot for left-handedness. No asymmetry in the funnel plot could be detected.*




*Supplementary Figure 4. Forest plot for left-handedness including the studies that did not have a clear IQ criterion.*




*Supplementary Figure 5. Funnel plot for mixed-handedness. No asymmetry in the funnel plot could be detected.*




*Supplementary Figure 6. Forest plot for mixed-handedness including the studies that did not have a clear IQ criterion.*

*Supplementary Table 1. Bayes factors (BFs) for different prior scales. For reports in the main manuscript, we used a prior scale of 0.3 as meta-analyses typically report small to medium effects.*

| Prior scale | Left-handedness BF10 | Mixed-handedness BF10 | Non-right-handedness BF10 |
|---|---|---|---|
| 0.3 | 2.46 | 22.7 | 25.57 |
| 0.5 | 1.63 | 17.89 | 18.40 |
| 0.707 | 1.19 | 13.97 | 13.76 |