**Can Cerebral Lateralisation Explain Heterogeneity in Language and Increased Non-right Handedness in Autism? A literature review.**

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**Abstract**

**Background**

Autism is characterised by phenotypic variability, particularly in the domains of language and handedness. However, the source of this heterogeneity is currently unclear.

**Aims**

To synthesise findings regarding the relationship between language, handedness, and cerebral lateralisation in autistic people and consider how future research should be conducted in order to progress our understanding of phenotypic variability.

**Methods and Procedures**

Following a literature search and selection process, 19 papers were included in this literature review. Studies using behavioural, structural, and functional measures of lateralisation are reviewed.

**Outcomes and Results**

The studies reviewed provided consistent evidence of differential cerebral lateralisation in autistic people, and this appears to be related to between-group differences in language. Evidence relating this to handedness was less consistent. Many of the studies did not include heterogeneous samples, and/or did not specify the language process they investigated.

**Conclusions and Implications**

This review suggests that further research is needed to fully understand the relationship between cerebral lateralisation and phenotypic variability within autism. It is crucial that future studies in this area include heterogeneous samples, specify the language process they are investigating, and consider taking developmental trajectories into account.

**Keywords**

Autism; cerebral lateralisation; language; handedness.

**What this paper adds**

This paper adds to our knowledge of the neurological underpinnings of the heterogeneity present in Autism, and provides suggestions for future research that will enable us to develop a clearer understanding of autistic cognition. We give an examination of the literature investigating the link between cerebral lateralisation, and heterogeneity of language and handedness in autism. We assess the suggestion that cerebral lateralisation underpins the heterogeneity seen in language ability and non-right handedness in autistic people, finding that there appears to be a consistent link between cerebral lateralisation of language and language ability in a range of domains (including expressive and receptive). The review suggests, however that these differences are not related to handedness, consistent with research suggesting that motor lateralisation is distinct from language lateralisation. We make recommendations for further research in this area, stressing the need for longitudinal and developmental trajectory designs that include heterogeneous samples (i.e. participants who use primarily linguistic vs. non-linguistic communication), and particular focus on the study of language in those with differential language lateralisation and motor organisation.

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1. **Introduction**

Autism is currently understood to be a form of neurodiversity, in which autistic people differ to the neurotypical (NT) population across a range of domains including perception, motor skills, social communication style and language (APA, 2013). The variability in which autistic characteristics are expressed across the autistic population is often referred to as phenotypic variability; one example is that some autistic individuals may demonstrate co-occurring learning disabilities (Matson & Shoemaker, 2009), or primarily non-linguistic forms of communication (Lombardo et al., 2015), whilst others may present fluent linguistic communication skills (Noterdaeme, Wriedt, & Höhne, 2010), however this variability is present across domains (i.e. sensory hyper vs. hypo sensitivity). Notably these abilities may also vary within an individual, with strengths and difficulties fluctuating with context. Historically, phenotypic variability was captured by the inclusion of two separate diagnostic categories: Autism (‘atypical’ language skills compared to NT peers), and Asperger Syndrome (‘typical’ to strong language skills compared to NT peers). However, in 2013 the DSM-V collapsed Autism, Asperger Syndrome, Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) and Childhood Disintegrative Disorder into a single diagnostic category using an umbrella term: Autism Spectrum Disorders (in this paper, we use ‘autism’). It is generally accepted that there are underlying neural differences between the autistic and NT populations. Indeed, many studies have been conducted with the aim of identifying links between cognitive, motor and perceptual differences between autistic and NT individuals in structural and/or functional brain development (Anderson et al., 2010; Arnold & Schwartz 1983; Blackstock, 1978; Floris, Barber, et al. 2016; Lindell, Notice, & Withers 2009; Lindell & Hudry, 2013).

Critically, although the diagnostic profile of autism is heterogenous, the differences in cognition between autistic and NT groups seem to occur predominantly in functions characterised by cerebral lateralisation. Cerebral lateralisation refers to the differential involvement of the left or the right cerebral hemisphere in specific cognitive processes (Hellige, 2001). For example, the left hemisphere is typically dominant for language and motor skills, while the right hemisphere is dominant for visuospatial processes (Broca, 1861; Hellige, 2001). A number of studies have demonstrated specific language differences in autism (Tager-Flusberg & Caronna, 2007; Boucher, 2012; Kjelgaard & Tager-Flusberg 2001), while others have demonstrated enhanced visuospatial processing abilities (Falter, Plaisted, & Davis 2008; Soulieres et al., 2011). It has been suggested that cerebral lateralisation may provide an explanation of the differences we see between autistic and NT populations (Lindell & Hudry, 2013). Here we specifically focus on an area that has received much attention; language. This review will explore the degree to which differences in cerebral lateralisation may explain heterogeneity in regards to language and handedness in the autistic population. It is important to note that no clear criterion exists regarding the degree at which cerebral lateralisation should be considered atypical, as laterality index-based cut-offs differ quite substantially across studies (Hodgetts & Hausmann, 2020; Vingerhoets, 2019; Hausmann, 2019); therefore, this review will refer to differences or heterogeneity in lateralisation as opposed to atypical or abnormal lateralisation.

Language differences are considered a core aspect of autism (Waterhouse, 2013), with research consistently demonstrating divergence with NTs in the developmental trajectory of both spoken and receptive verbal ability (Hudry et al., 2010). There is strong evidence from both neuroimaging (Everts et al., 2009; Jancke et al. 2001) and behavioural (Hirnstein et al., 2014; Hugdahl, 1995; 2003) studies demonstrating that language is lateralised to the left hemisphere in NT individuals, including core language regions such as Broca’s area and the default mode network (Nielsen et al., 2014). This does not seem to be the case in autistic people (Lombardo et al., 2015). Moreover, a significant body of evidence suggests that autism is also characterised by different patterns of handedness (Markou, Ahtam, & Papadatou-Pastou 2017; Preslar et al. 2014; Rysstad & Pedersen 2016) which further suggests that cerebral lateralisation may underpin the phenotypic variabilities seen in autism.

* 1. *Handedness and Language Lateralisation**in Neurotypicals*

The prevalence of right-hand dominance in the neurotypical population is estimated at around 90% (for a review, see McManus & Bryden, 1992). Furthermore, it is thought that handedness presents an easy-to-measure indicator of cerebral lateralisation of language. The organisation of language to the left hemisphere is one of the most reliable findings in the field of laterality (Hugdahl 2000; Ocklenburg & Güntürkün 2012). A number of clinical observations suggested that there may be inter-individual differences in language lateralisation. For example, while most patients with aphasia have damage to the left cerebral hemisphere, it is estimated that around 10% of aphasic patients have experienced damage to the right hemisphere (McManus, 1999). Early explanations for this finding suggested that handedness played a mediating role in language lateralisation. Specifically, while language is lateralised to the left hemisphere in right-handed individuals, the opposite was true for left-handed individuals (Strauss & Wada, 1983).

However, further findings suggest that the relationship between handedness and language lateralisation is more complex than initially suggested. There is evidence from behavioural (Bryden, 1988; Moncrieff, 2011) and functional neuroimaging paradigms (Knecht et al. 2000) demonstrating right-hemispheric language lateralisation in a subset of NT right-handed participants. Still further research suggests that the majority of NT left-handed (and ambidextrous/non-right handed) participants are lateralised to the left hemisphere for language (Pujol et al., 1999; Szaflarski et al., 2002; Szaflarski et al., 2012). Taken together, these findings suggest that the majority of right-handers (approximately 95%) *and* most left-handers (approximately 70%) are lateralised to the left hemisphere for language (McManus, 2019). Several theories have been developed attempting to explain right hemispheric lateralisation for language, and a full discussion of these theories is beyond the scope of the current review (see McManus, 2019 for a comprehensive review of handedness research to date).

* 1. *Handedness, language ability, and lateralisation**in autism*

Elevated prevalence of non-right hand dominance (i.e. left-handedness or mixed-handedness/ambidexterity) has been frequently reported in autistic people, relative to the NT population (Markou, Ahtam, & Papadatou-Pastou, 2017; Preslar et al., 2014; Rysstad & Pedersen, 2016). Rysstad and Pedersen (2016) reviewed handedness data from 497 autistic participants, which demonstrated increased instances of left-handedness, and mixed-handedness. A meta-analysis from Markou, Ahtam, and Papadatou-Pastou (2017) yielded concurrent results, reporting that autistic individuals are 3.48 times as likely to be non-right hand dominant, 2.49 times as likely to be left handed and 2.34 times as likely to be mixed handed compared to NT individuals. Moreover, Markou et al. (2017) suggest that differences in handedness may be indicative of differential cerebral lateralisation, which in turn may explain language heterogeneity within the autistic population.

A similar notion was suggested by Lindell and Hudry (2013). The authors reviewed the relationship between language, handedness, and differential cortical lateralisation in autism. Subsequently, they proposed a model to explain the relationship between reduced structural and functional lateralisation and language with handedness as a moderating factor. The model describes a combination of genetic and environmental factors that exert an interactive influence on lateralisation from birth, which results in reduced structural lateralisation of the brain, and non-right hand dominance or mixed handedness. This differential handedness profile leads to bilateral (as opposed to lateralised/asymmetrical) cerebral organisation, which in turn results in reduced functional lateralisation (i.e. for language).

Critically, the authors acknowledge that their review does not explicitly address heterogeneity in autism. This is primarily due to the nature of autism research at the time that the article was published. Specifically, the majority of research in this period was focused on developing a unifying theory of autism as a whole, rather than understanding phenotypic variability. Consequently, the authors stress the need for more longitudinal research in order to examine developmental trajectories for cerebral lateralisation and associated cognitive skills. They also identify the need for more research into the Broader Autism Phenotype (BAP (Wheelwright et al., 2010), to provide an understanding of the genetic contribution to the language differences we see in the autistic population.

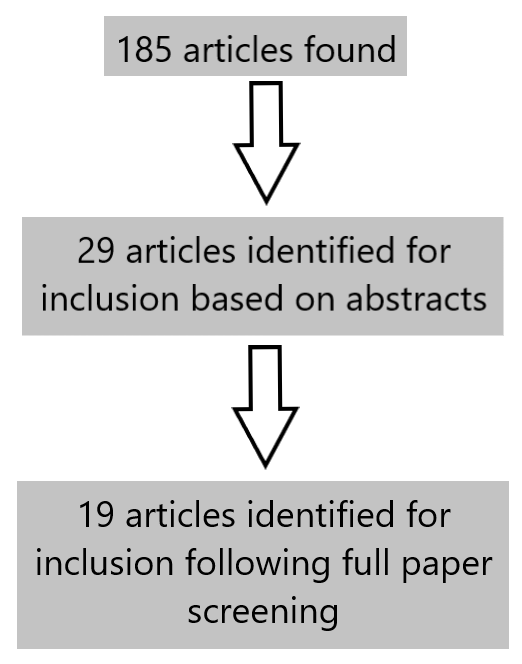
These studies suggest that non-right hand dominance and language heterogeneity in autism may relate to differential hemispheric lateralisation compared to NT individuals (Marokou et al., 2017). However, more evidence is required to address sources of heterogeneity (Lombardo, 2019). The aim of this review is to build upon the work of Lindell and Hudry (2013) and Preslar et al. (2014), to provide a comprehensive, critical examination of the literature concerning the relationship between handedness and language in autistic people, and consider how inconsistencies can be addressed in order to try and gain a deeper understanding of phenotypic variability in autistic people.

1. **Methodology**

The literature search was conducted by the first author using Medline-Pubmed. To identify papers, the keywords ‘autism’, ‘handedness’, ‘laterality’ and ‘language’ were entered into the PubMed database, which returned a total of 185 papers. Initial inclusion criteria were:

1. The abstract of the article was published in English in a peer-reviewed journal;
2. The study used a behavioural measure of language, including either a cognitive battery with a verbal component such as the Wechsler scales, or a cognitive language task.
3. The sample included autistic children or adults, or a measure of the Broader Autism Phenotype (BAP).
4. The study did not receive previous attention in the 2013 review from Lindell and Hudry.
5. Handedness of the participants was reported.

From the 185 papers returned in the initial search, abstracts were assessed for evidence of inclusion criteria, and the papers checked against the reference list given in Lindell and Hudry (2013), which resulted in 29 potential papers. Both authors then read the remaining papers in detail, and rejected 10 further papers: one that upon closer inspection did not report or measure handedness (Gunter, Ghaziuddin, & Ellis 2002), one that did not take an objective measure of language ability (Bonvillian et al., 2001), seven that did not mention handedness beyond the method section (Gao et al. 2019; Ji et al. 2019; Jouralev et al. 2020; Yeung et al. 2019; Hillus et al. 2019; Grisoni et al. 2019; Roberts et al. 2019), and one that had not undergone peer review (Floris et al. 2020. This resulted in a final sample of 19 papers, published between 1982-2020. As such, the current review included a number of more recent studies, as well as studies that were excluded from the meta-analysis reported by Preslar et al. (2014).



**Figure 1.** Study identification and selection process

1. **Results**
   1. *Description of studies*

Across the 19 studies, there were a total of 708 (133 female) autistic participants and 622 (111 female) non-autistic participants. Most of the studies included at least one comparison group, with one exception examining within-group phenotypic variability in a large (205) sample of autistic children (Oslejskova et al., 2007). Six studies examined adults (Floris et al., 2016; Kasai et al., 2005; Martinez-Sanchis et al., 2014; Mason et al., 2008; McFadden et al., 2012; Rumsey & Hamburger, 1988), four examined adolescents (Cardinale et al., 2013; Cardy et al., 2008; Hoffmann & Prior 1982; Knaus et al., 2008), and nine examined children (Chandana et al. 2005; Finch et al., 2017; Gillberg, 1983; Joseph et al., 2014; Knaus, Kamps, & Foundas, 2016; Minagawa-Kawai et al., 2009; Noterdaeme et al., 2002; Oslejskova et al., 2007; Dimitrova, Mohr, Özçalışkan and Adamson., 2019).

Intelligence quotients (IQ) were reported in 12 studies, however two of these did not report the IQ of the NT group (Kasai et al., 2005; Minagawa-Kawai et al., 2009). Whilst the majority of studies reported IQ scores above 70, two reported autistic group averages in the 50’s (55 and 57.2 in children and adults studied by Oslejskova et al. (2007) and Kasai et al., (2005), respectively). One of the studies specifically used the label ‘high functioning’ autism (Rumsey & Hamburger, 1988), whereas others specified that they used a varied sample to examine phenotypic variability, usually in those with and without delayed language development.

Four studies included right-handed participants only (Floris, Lai, et al. 2016; Kasai et al. 2005; Knaus et al. 2008; Minagawa-Kawai et al. 2009); one included right-handers and left-handers, but performed MRI on right-handers only (Noterdaeme et al., 2002), and the remaining 14 included both right, left and mixed handed participants. Handedness was assessed using a variety of different measures (see Table 1), including the Almli Handedness Assessment (Knaus, Kamps, & Foundas 2016), Edinburgh Handedness Inventory (Cardinale et al.. 2013; Floris et al., 2016; Kasai et al. 2005; Martinez-Sanchis et al., 2014; Minagawa-Kawai et al., 2009), Dean Handedness Inventory (Joseph et al., 2014; Knaus et al., 2008), Annett Handedness Test (McFadden et al., 2012), self-report (Chandana et al., 2005; Rumsey & Hamburger, 1988), gesture indexing (Dimitrova et al. 2019) and neuropsychological indicators of handedness (Mason et al., 2008; Noterdaeme et al., 2002; Oslejskova et al., 2007), such as the Purdue pegboard task. Some of these measures give handedness direction (left/right/mixed), whereas others give strength (indicator of strong right handedness, as in the EHI).

Cerebral lateralisation was estimated using a variety of different measures across the studies we report. In the structural imaging studies, most use some variation of the formula: (Left volume–Right volume)/[(Left volume+Right volume)×.50]. Estimates vary across the functional imaging studies, with most examining differences in activity between the left and right hemisphere.

* 1. *Behavioural Evidence of Cerebral Lateralisation Differences*

Left hemisphere dysfunction was a popular explanation of the language and handedness differences seen in autism during the 1970’s and 1980’s (Lindell and Hudry 2013). Three of the papers included here examined the left hemisphere dysfunction hypothesis. Hoffmann and Prior (1982) conducted a battery of neuropsychological tests with autistic children compared to a group of age and IQ matched NT children. No significant differences were found in handedness or lateralisation between the groups. However, there was evidence of lower language ability (WISC Vocabulary, Comprehension, and Similarities subtests) in the autistic children, taken as evidence of a possible left hemisphere dysfunction. The two remaining studies found little evidence to support this assertion. Rumsey and Hamburger (1988) examined neuropsychological differences between a group of autistic adult males and a group of age and gender matched NT adults. There was a higher prevalence of non-right handedness in the autistic group (assessed using self-report). Results of the neuropsychological battery revealed lower language performance in the autistic participants, despite participants being in the above average verbal IQ range. No associations were found with handedness, and autistic participants did not display behavioural evidence of weaker motor lateralisation compared to the NT group. Gillberg (1983) examined instances of increased non-right handedness in autistic children compared to a group of age, gender and IQ matched NT children. Results showed higher rates of non-right handedness in the autistic children, which was associated with developmental language differences (i.e. echolalia). Neither of these studies provide a link between handedness and language heterogeneity in autistic children, however both do make the suggestion that differences in a wider network of brain regions could be implicated in any differences and acknowledge the role of hemispheric lateralisation in both of these outcomes.

More recently, several studies have provided behavioural evidence of lateralisation differences in autistic people. Noterdaeme et al. (2002) did not directly measure language lateralisation, however their study on neuromotor differences included a measures of language skills alongside handedness in four groups: autistic children, children with receptive Language Impairments (LI), expressive LIs and NT children all matched for non-verbal IQ performance. There were no significant differences in handedness across the groups; there were four left handed children (one with expressive LI, two receptive LI and one autistic) in the whole sample. Thus, results of this study do not suggest handedness is related to language heterogeneity in either autistic children, or those with other LIs. Dimitrova et al (2019) examined whether gesture production, handedness and expressive speech production are related in autistic and NT children. They observed gesture production in parent-child interactions, and coded the strength of hand preference by calculating a handedness index using the formula [(R−L)/(R+L)]. For handedness, they found that comparable numbers of autistic and NT children showed strong right hand preference, but that more autistic children showed more mixed or strong left handedness, whereas more NT children showed mixed right handedness. For gesture, they found that right hand gesture production predicted expressive speech production at a 1 year follow up in both autistic and NT children, and that left hand gesture production predicted expressive speech production in NT children only. Handedness indices did not predict expressive speech in either group. The authors suggest that the lack of a right hand preference in the autistic children may indicate a reduced left hemispheric dominance for language, but acknowledge that without neuroimaging data this is speculative.

More direct evidence implicating cerebral lateralisation in language-handedness heterogeneity relationship in autism comes from Knaus, Kamps, and Foundas (2016). This study investigated language-handedness associations in age matched autistic and NT children. Children completed the Almli Handedness Assessment, the Mullen Scales Early Learning (MSEL, Mullen 1995) and the Oral and Written Language Scales (OWLS, Carrow-Woolfolk 1995). The NT children had significantly higher expressive and receptive language scores than the autistic children, and displayed higher rates of right hand dominance. The autistic children had weaker hand preferences than the NT children, and had increased instances of left and mixed handedness. There were no across group correlations between handedness and language. However, at the individual group level, the right-handed autistic children tended to have higher receptive and expressive language scores, whereas no such relationship was found in the NT children. When the autistic group was split into average/above average and low for expressive language, authors also found higher handedness scores (indicating stronger cerebral lateralisation for motor processes) in the average/above group compared to the low group. These findings were not replicated for receptive language. These findings indicate support for lateralisation contributing towards expressive language heterogeneity in autistic children, and a relationship between early differential language lateralisation and handedness. The results of this study are important as they demonstrate a relationship between expressive language heterogeneity and lateralisation (using handedness as a proximal measure), but not receptive. The majority of studies on language, lateralisation and handedness include participants who do not have co-occurring learning disabilities, and use primarily spoken means of communication. In sum, Knaus et al. 's (2016) findings suggest that making assumptions about understanding of language based on expressive verbal measurements is problematic.

* 1. *Structural Evidence of Cerebral Lateralisation Differences*

As with behavioural findings on the relationship between language, handedness and lateralisation, structural evidence (from neuroimaging studies) of lateralisation differences between autistic participants and NTs is inconsistent. All three structural studies we include found between-group differences in cerebral lateralisation, but the relationship with handedness was weak or non-existent. Chandana et al. (2005) used PET to examine structural asymmetry in a large (n=117) group of autistic children compared to a small group of NT (n=8) children. The Vineland Adaptive Behaviour Scales (VABS, Sparrow 1989) was used to assess language in the autistic but not NT children, however the sample did include children with a range of linguistic ability (low, average and high scoring) suggesting that heterogeneity was present in the sample. Handedness was measured using parental self-report. Children were divided into groups on the basis of cortical asymmetry, inferred from measures of AMT update (a measure of serotonin synthesis). Results indicated that autistic children with decreased AMT uptake in the left hemisphere had higher incidences of specific language impairment compared to those with a right hemispheric decrease and no asymmetry groups. There was no overall relationship between cortical asymmetry and handedness, however there was a trend towards increased left or mixed handedness in the right-decrease group. Findings suggest that neurochemistry may be an attenuating factor in differential structural asymmetry that may contribute towards aspects of language development. Further evidence for a left hemisphere decrease was found by Floris et al. (2016), who examined hemispheric asymmetry in right-handed autistic adults compared to age and IQ matched NT adults. Participants completed the two language tasks: the FAS (Gladjso et al., 1999) and the nonword repetition task, as well as the Purdue Pegboard task (to assess motor dexterity), and an Embedded Figures task. Participants also underwent structural MRI, with regions of interest (ROIs) defined as Broca's area, the planum temporale (PT), precentral gyrus (PCG), and inferior parietal lobule (IPL). Results showed that autistic participants with language delay had reduced leftward asymmetry and reduced language lateralisation compared to those without language delay, suggesting that lateralisation differences might explain language heterogeneity. Though these findings are consistent with those of Escalante-Mead, Minshew, & Sweeney (2003), the authors only tested right-hand dominant participants, and so it is difficult to draw conclusions on handedness. Though the sample included participants with language delay, none of the participants had co-occurring learning disabilities, thus examination of longitudinal heterogeneity was not possible. This is a common problem in autism research; there is a distinct lack of inclusion of individuals with co-occurring learning disabilities, particularly those that might display primarily non-linguistic communication in adulthood. If our understanding of communicative heterogeneity in autism is to be fully explored, studies need to include participants who use primarily non-linguistic means of communication.

Joseph et al. (2014) used MRI to examine structural asymmetry in autistic children compared to NT children. The two groups were not matched for age or IQ. Children were assessed for language ability using the Differential Ability Scales (DAS, Elliot, 1990) and OWLS, and handedness. ROIs were the PT, superior temporal gyrus (STG), pars opercularis (POP), and pars triangularis (PTR). Structural scans revealed no differences in gray matter asymmetries between groups, however the relationship between these asymmetries and language differed between groups, with the autistic children showing a positive association between rightward asymmetry of the pars opercularis and language ability as measured by the DAS. These findings however were independent of handedness. There were no differences between groups in asymmetry of the planum temporale, an area previously associated with between-group differences in language (Eckert, Lombardino, & Leonard 2001). There were group differences in white matter, autistic children also had less leftward volumetric asymmetry, however these differences were not associated with language. These findings are inconsistent with previous findings showing that rightward asymmetry was associated with poorer language outcomes in autistic children (Lombardo et al., 2015), however children in Josephs study had been enrolled in an early (unspecified) intervention. These results suggest that structural asymmetry does not necessarily determine language outcomes in autistic children. Findings are consistent with the suggestion that stronger hemispheric lateralisation for language is more beneficial than bilateral distribution, regardless of direction (Bryden, Hécaen, & DeAgostini, 1983).

* 1. *Functional Neuroimaging Evidence of Cerebral Lateralisation Differences*

Evidence from functional neuroimaging appears to be much more consistent than behavioural or structural studies. Two studies we reviewed found a small link between handedness and speech lateralisation in autistic participants. (Finch et al., 2017; Oslejskova et al., 2007). Oslejskova et al. (2007) examined the relationship between neurological differences, handedness and language ability in a sample of 205 autistic children. Sixty percent of their sample were non-right hand dominant, and participants showed heterogeneity in regards to language and general cognitive ability. The authors examined several functional language domains including speech regression, delayed development, and structural aspects of language. Results suggested that non-right handedness and a lower IQ score were related to speech issues across domains. It is worth noting however that many of the participants in this study were diagnosed with epilepsy, which is also related to non-right handedness and language ability. There is still little research into the relationship between autism and co-occurring epilepsy, and the role that this plays in cognitive heterogeneity. Finch et al. (2017) examined the relationship between language lateralisation and handedness in a longitudinal study with children that were classified as autistic (initially classified as ‘high risk for autism’ (HRA) on the basis of having an older autistic sibling), HRA controls who did not go on to gain a diagnosis, and neurotypical ‘low-risk’ controls (LRC). Infants underwent ERP recordings while listening to speech at 12 months, and handedness was assessed at 36 months during a follow-up using observations of dominant hand use during the Autism Diagnostic Observation Schedule (ADOS, Lord et al., 1989) and MSEL. Results showed that those diagnosed as autistic at 36 months had reversed lateralisation for speech sounds at 12 months, including those without language delays, as compared to LRC children. These findings suggest that language heterogeneity in autistic children cannot be simplified to differential early cerebral lateralisation, as suggested in Lindell and Hudry’s (2013) model. However, Finch et al. (2017) also acknowledged that all but two of the children in their sample had average or above average performance on the MSEL at 36 months, indicating that there was a lack of language heterogeneity in their autistic group. This could also account for the higher levels of right hand dominance displayed in their autistic group, as higher proportions of mixed or non-right hand dominance also tend to be found in people with co-occurring learning disabilities (Soper et al., 1986). The authors found no relationship between speech lateralisation at 12 months and handedness at 36 months, however they did find that autistic children whose speech lateralisation was more similar to that of LRC at 12 months were more likely to be right handed at 36 months. These findings do support the notion proposed by Lindell and Hudry (2013) that handedness may in some way mediate the link between genetic and environmental factors, and structural lateralisation. However differential speech lateralisation was not found in the HRA infants, making it difficult to make assumptions about genetics or environment (given that both were shared with autistic siblings), and reversed attenuation to speech sounds did not appear to result in observed language impairments at the later point in the autistic group, suggesting that differential cerebral lateralisation does not consistently result in linguistic difficulty.

The six remaining studies found consistent lateralisation differences between autistic and comparison samples in relation to speech and language, but no evidence of these differences being mediated by handedness. Kasai et al. (2005) used MEG to examine functional speech lateralisation using auditory magnetic mismatch field (MMF) in right-handed (assessed using the EHI) autistic and age and handedness matched NT adults. Full-scale IQ scores in the autistic group ranged from 37-71, suggesting that this study captured a wider range of participants than other studies. Participants were presented with pure tone, vowel (phoneme-duration) and vowel (across-phoneme) stimuli. The autistic participants showed delayed latency of the MMF in the left hemisphere in the across-phoneme condition, associated with higher scores on the Childhood Autism Rating Scale (Schopler et al. 1980) but not IQ. Additionally, MMF latency in the right hemisphere was related negatively to IQ in the phoneme-duration condition in the autistic group. These results suggest that differential lateralisation is related to heterogeneity in autism, though not specifically for language. It must be noted here however that individual scores of verbal performance were difficult to attain due to multiple measures used to gauge IQ, and the autistic sample (n=9) was particularly small. Several studies found rightward shifts or increased rightward lateralisation of speech and language. Cardy et al. (2008) used MEG to examine functional lateralisation in autistic children (one left handed), children with Specific Language Impairment (SLI) and NT children (one left handed). For the purpose of analysis, participants were grouped by history of LI. Results demonstrated that auditory response latencies predicted receptive verbal ability in children with LI (both autistic and SLI), indicating differential lateralisation of language in the right cerebral hemisphere. Though the data are not causal, they support the notion of Lindell and Hudry that differences in structural lateralisation might lead to linguistic difficulties. Their data suggest that these findings might be cross-condition, pointing to a shared mechanism for language heterogeneity in neurodiverse populations (here autistic and SLI).

Mason et al. (2008) examined functional lateralisation and connectivity across multiple ROIs during narrative comprehension in autistic adults and a group of age and IQ matched NT adults. All participants were right handed, with the exception of three of the autistic adults who were left handed. All participants completed a narrative comprehension task in which they responded to questions about physical, intention and emotional inferences while undergoing fMRI. Results showed differences in functional connectivity between the autistic and NT participants. The autistic group displayed weaker connectivity between areas engaged in mentalising and language in the left hemisphere, and increased right hemisphere activity during these tasks which the authors argue may be compensatory (however this may simply be evidence of differential lateralisation). Cardinale et al. (2013) also found evidence of increased rightward activity in their sample. They examined functional asymmetry using resting state fMRI in autistic children and adolescents compared to a group of age, handedness and IQ matched NT individuals. In addition to rightward shifts of activity seen in the autistic children, the authors found a significant correlation between leftward activity of the frontoparietal regions and verbal IQ scores. Notably leftward asymmetry was found only in the NT group, the autistic group showed more bilateral activity. No associations were found with handedness. Results are supportive of the suggestion that differential language lateralisation is not limited to autistic children with SLIs.

Two studies found weaker evidence for aspects of language heterogeneity relating to cerebral lateralisation. Minagawa-Kawai et al. (2009) used NIRS to examine functional lateralisation in right handed autistic and NT children. The autistic sample included children with and without co-occurring learning difficulties. Children listened to Japanese phonemic and prosodic stimuli while undergoing bilateral recording of auditory areas using NIRS. A group by task interaction revealed that the autistic children showed weaker lateralisation compared to the NT children in the phonemic condition, but not the prosodic. No correlation was found between age, IQ, or handedness in either sample. Knaus et al. (2008) examined functional lateralisation in frontal and medial language areas using fMRI in a group of male autistic adolescents compared to a group of gender, age and handedness (right handed only) matched NTs. Participants completed measures of IQ, expressive and receptive language ability, and underwent fMRI whilst performing a response-naming, and letter-judgement task. Results showed that the autistic participants were both faster and more accurate in the response naming and letter judgement tasks. The autistic group displayed reduced lateralisation, but stronger activation in Broca’s area compared to NT participants, and fronto-temporal activation in the left hemisphere was correlated in NT participants, but not autistic, indicative of differential functional connectivity in this group. There were no correlations with functional asymmetry and IQ, or expressive and receptive verbal performance in either group.

* 1. *Lateralisation in the Broader Autism Phenotype*

Three studies examined cerebral lateralisation in the BAP in relation to handedness and language in groups of non-autistic adults. Martinez-Sanchis et al. (2014) tested parents of autistic children using a dichotic listening task alongside a measure of empathy (the Empathy Quotient, Baron-Cohen and Wheelwright, 2004) and handedness. There was a significant right ear advantage (indicative of left hemisphere language processing) across participants and no correlation between ears. However, when analysed by gender, mothers right ear data was significantly negatively correlated with left ear data, whereas fathers showed no correlation. Twenty two participants were right handed, one mother was left handed, and one mother and one father were ambidextrous, thus the relationship between handedness and the dichotic listening task was unexplored due to a lack of variability in the handedness data. The authors suggest that the lack of hemispheric interdependence found in the fathers is similar to lateralisation differences found in autism, suggesting a genetic component to heterogeneity. However, the sample was too small to explore this further. McFadden et al. (2012) examined lateralisation in response to language stimuli in the BAP, testing parents of autistic children compared to a group of age, handedness and IQ matched NT adults with no family history of autism diagnosis. Participants completed measures of receptive and expressive verbal fluency, as well as figurative language and phonological processing, as well as undergoing MEG while completing a continuous word recognition task. Compared to NTs, the BAP group showed lower performance in continuous word recognition, and a trend towards lower receptive verbal ability. MEG revealed that the BAP group had increased gamma wave activity and increased left lateralisation of language compared to the NT group. There were several differential relationships found between gamma/beta activity and performance on each of the language measures across groups, particularly in the expressive and receptive language measures which is consistent with research from Knaus, Kamps, and Foundas (2016).

1. **Discussion**

The studies reviewed here show inconsistent evidence as to whether cerebral lateralisation can explain heterogeneity in speech and language, and increased non-right handedness in autistic people. The studies reviewed here were consistent with those reviewed by Lindell and Hudry (2013) in providing evidence of differential structural cortical organisation in autistic compared to NT individuals, which appears to be related to language. However, the studies we review here show weak/no relationship with structural differences and non-right handedness. Functional neuroimaging evidence somewhat supported these findings. These studies showed a more consistent relationship between language lateralisation and language ability, but only two studies found that these differences were related to non-right handedness (Finch et al., 2017; Oslejskova et al., 2007). Oslejskova et al. (2007) had a larger and more heterogeneous sample than some others reviewed, however their results were confounded by the presence of co-occurring diagnoses (epilepsy). Finch et al. (2017) was lacking in sample heterogeneity, however their longitudinal data does provide a more meaningful understanding of the trajectory for functional lateralisation differences and language development may take in autistic people. Their data suggest that non-right handedness is associated with language, but the relationship is not straightforward. The remaining functional studies reviewed provided no evidence of a relationship between language, functional lateralisation, and non-right handedness.

Though many of the studies reviewed lacked within-sample heterogeneity, across-study heterogeneity was present. Across these studies, it appears that language lateralisation is a key factor in understanding language heterogeneity in autism and the BAP, but the relationship with non-right handedness is not clear. Groen et al. (2013) assessed the use of handedness as a behavioural indicator of cerebral lateralisation for language in NT children, finding that is a particularly weak indicator. Additionally, the authors suggest that lateralisation of language and motor skills appear to be independent, questioning the possibility of a mediating role of handedness suggested by Lindell and Hudry (2013). These findings suggest that cerebral lateralisation as an explanation of heterogeneity in autism may need to be considered in a more general manner in order to provide a bigger picture of the differences. Increased instances of non-right handedness, particularly in those with ‘poorer’ language outcomes seems unlikely to be a direct relationship, in which mixed handedness drives structural/functional development and leads to difficulties. Instead, it is likely that those with both differentially lateralised motor and language abilities are more likely to display non-right handedness. Rather than asking whether higher prevalence of non-right hand dominance is related to language heterogeneity in autistic people, we suggest that researchers consider language ability in people who have differential language lateralisation and differential motor organisation.

This being said, several key issues were identified during this review that need to be addressed if future research into cerebral lateralisation and language with autistic people is to provide any consistent understanding. Firstly, researchers need to be clear in defining which aspects of language in autistic people appear to be heterogeneous, and how different aspects of language may be related. Research reviewed here suggests that there may be differences between receptive and expressive verbal ability with autistic groups; thus we suggest that more research is required to examine which specific aspects of language are heterogenous, and how these may relate to differences in implicated neural systems. Practically speaking, if research is to provide meaningful understanding as to why some autistic people use primarily non-linguistic communication, then clear demarcations between different aspects of language heterogeneity need to be established. If there are within-autistic differences in receptive and expressive linguistic ability, these can help us to establish alternative pathways for assisting communication (i.e. sign-language or augmentative and alternative communication, or AAC). Secondly, further research must include a heterogeneous sample if it is to examine heterogeneity. The studies reviewed here that had more heterogeneous samples (Chandana et al. 2005; Knaus, Kamps, and Foundas 2016; Oslejskova et al. 2007) display clear relationships between language lateralisation and heterogeneity, which points towards a need for further investigation. Finch et al (2017) also demonstrates the value of longitudinal research in this area, as this will provide a clearer understanding of the developmental trajectory of the relationship between cerebral lateralisation and language heterogeneity. In addition to longitudinal research, studies using a developmental trajectory approach with different age groups would provide knowledge about these relationships across the lifespan. Based on the evidence provided by the studies reviewed here, the model provided by Lindell and Hudry does not appear to be sufficient for explaining language and handedness heterogeneity in autism. Floris and Howells (2018) suggest that differential lateralisation (in the motor domain) might allow for investigation of phenotypic ‘subtypes’ in autism. We do not endorse this notion as a way to approach understanding heterogeneity in neurodivergent people. Firstly, it does not take into account factors such as identified and unidentified co-occurring diagnoses and how poorly constructed the boundaries between different diagnoses are (Allsopp, read, Corcoran and Kinderman., 2019). Secondly, attempting to create discrete subtypes in neurodivergent people based on limited measures and external observation, will likely lead to more fragmented and inconsistent research. Ideally, future research would draw upon understanding gained from studies on language lateralisation to support the development of personal communicative preference in autistic people.

1. **Conclusion**

The findings distilled in this review suggest that investigation of cerebral lateralisation in autistic people may provide a deeper understanding of the nature of cognitive phenotypic variability in (but not limited to) this population. Further research is needed that examines the structural and functional differences in left and right lateralised abilities (i.e. language and motor skills), using longitudinal and developmental trajectory samples. It is also imperative that cognitive researchers clearly specify which processes they are investigating (i.e. expressive or receptive language), include heterogeneous samples in their studies in order to provide evidence from under-studied populations, and that co-occurring diagnoses are also taken into account.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Year** | **(n) Autistic** | **(n) NT** | **Age Autistic** | **Age NT** | **IQ Aut** | **IQ NT** | **Handedness** | **Handedness Measure** |
| Hoffman and Prior | 1982 | 10 | 10 CA  10 MA | 11.3 | 11.3  8.9 | 87 | 100  107 | Mixed | NPB |
| Gillberg | 1983 | 26 | 52 | N/A | N/A | N/A | N/A | Mixed | Annett |
| Rumsey and Hamburger | 1988 | 10 | 10 | 26 | 28 | 103 | 112 | Mixed | Self-report |
| Noterdaeme et. al | 2002 | 11 | 11 | 9.8 | 8.1 | 103 | 105 | Mixed | NPB |
| Kasai et al. | 2005 | 9 | 19 | 27.2 | 27.3 | 57.2 | N/A | RH only | EHI |
| Chandana et al. | 2005 | 117 | 8 | 6.5 | 9.2 | N/A | N/A | Mixed | Self-report |
| Oseljskova et al. | 2007 | 205 | N/A | 10 | N/A | 55 | N/A | Mixed | Self-report |
| Mason et al. | 2008 | 18 | 18 | 26.5 | 27.4 | 101 | 105 | Mixed | NPB |
| Cardy et al. | 2008 | 24 | 16 | N/A | N/A | N/A | N/A | Mixed | Self-report |
| Knaus et al. | 2008 | 12 | 12 | 15.46 | 14.94 | 105 | 122 | RH only | DHI |
| Minagawa-Kawai et al. | 2009 | 13 | 7 | 9.2 | 7.3 | 70+ | N/A | RH Only | EHI |
| McFadden et al. | 2012 | 23 | 28 | 38.7 | 35.8 | 115 | 117 | Mixed | Annett |
| Cardinale et al. | 2013 | 20 | 20 | 14.6 | 14.7 | 114 | 108 | Mixed | EHI |
| Martinez-Sanchis et al. | 2014 | N/A | 25 | N/A | N/A | N/A | N/A | Mixed | EHI |
| Joseph et al. | 2014 | 20 | 20 | 5.11 | 9.4 | 93 | 117 | Mixed | DHI |
| Knaus, Kamps and Foundas | 2016 | 110 | 45 | 8.3 | 8.6 | 93 | 117 | Mixed | Almli |
| Floris et al. | 2016 | 67 | 69 | 26.2 | 27.9 | 108.7 | 108.8 | RH Only | EHI |
| Finch et al. | 2017 | 23 | 73 ‘Low risk’  67 ‘High risk’ |  |  |  |  | Mixed |  |
| Dimitrova et al. | 2019 | 23 | 23 | N/A | N/A | N/A | N/A | Mixed | Gesture index |

**Table 1:** Demographic descriptions of the studies included in the literature review