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# Variability in lateralised blood flow response to language is associated with language development in children aged 1–5 years

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ABSTRACT

The developmental trajectory of language lateralisation over the preschool years is unclear. We explored the relationship between lateralisation of cerebral blood flow velocity response to object naming and cognitive performance in children aged 1–5 years. Functional transcranial Doppler ultrasound was used to record blood flow velocity bilaterally from middle cerebral arteries during a naming task in 58 children (59% male). At group level, the Lateralisation Index (LI) revealed a greater relative increase in cerebral blood flow velocity within the left as compared to right middle cerebral artery. After controlling for maternal IQ, left-lateralised children displayed lower expressive language scores compared to right- and bi-lateralised children, and reduced variability in LI. Supporting this, greater variability in lateralised response, rather than mean response, was indicative of greater expressive language ability. Findings suggest that a delayed establishment of language specialisation is associated with better language ability in the preschool years.



## 1. Introduction

Studies in children show language is lateralised to the left hemisphere of the brain from six years of age (e.g. see Groen, Whitehouse, Badcock, & Bishop, 2012). Studies in clinical populations with reduced language skill suggest such functional specialisation is associated with greater cognitive performance (de Guibert et al., 2011; Everts et al., 2010; Flagg, Cardy, Roberts, & Roberts, 2005; Jacola et al., 2006; Johnson et al., 2013; Spironelli, Penolazzi, Vio, & Angrilli, 2006). When such lateralisation develops earlier in life and the trajectory of any such development is not clear. Traditionally, models have suggested underlying genetic risk by which weak laterality causes delayed or impaired language function, or which independently impairs both laterality and language (Annett, 1985; Bishop, 2013). However, such models have received limited support from studies investigating the heritability of functional brain asymmetry to language tasks, and those targeting candidate genetic variants (for review see Bishop, 2013).

Another view is that asymmetries to language reflect a maturational process, confined by genetic boundaries but largely defined by experience. Minagawa-Kawai, Cristia, and Dupoux (2011) proposed a model whereby lateralised language function begins very early in development as asymmetrical activation to different sounds, specifically rapid changing sounds yielding a left- or bi-lateral activation. After this, newly learned sounds are captured in the left-dominant phonetic and lexical circuits, typically giving rise to left-lateralised language networks. Consistent with this idea is the observed developmental trajectory of left lateralisation to phonological contrasts in an infant's native language (Arimitsu et al., 2011; Furuya, Mori, Minagawa-Kawai, & Hayashi, 2001; Minagawa-Kawai et al., 2009; Sato, Sogabe, & Mazuka, 2007; Sato et al., 2003). As well, studies in older children and adolescents demonstrating a left lateralisation to lexical–sematic tasks compared to more distributed or bilateral activation for syntactically-loaded tasks (Holland et al., 2007).

Studies in healthy populations of older children, typically from about school age onward, strongly support a left dominant activation in normal language development. fMRI paradigms in school aged children and adolescents typically show a predominant left hemisphere activation for silent word generation tasks (Norrelgen, Lilja, Ingvar, Gisselgard, & Fransson, 2012; Szaflarski

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et al., 2012; Wood et al., 2004), silent reading (Gaillard, Balsamo, Ibrahim, Sachs, & Xu, 2003) and an auditory categorisation task (Balsamo, Xu, & Gaillard, 2006) in areas of the frontal and temporal gyri as well as fusiform and supplementary motors area. In addition, a number of these studies have indicated a positive correlation between left activation and task performance (Balsamo et al., 2006; Wood et al., 2004). Magnetoencephalography (MEG) studies with children and adolescents aged 5–19 years have also shown a predominant left lateralisation to word generation tasks but, unlike in fMRI studies, one that increases in prominence with age between around 5–7 years and mid-late adolescence (Balsamo et al., 2006; Kadis et al., 2011; Ressel, Wilke, Lidzba, Lutzenberger, & Krageloh-Mann, 2008; Wood et al., 2004).

When conducting functional imaging studies in young children, compliance with instruction to remain very still for extended periods without the possibility of close caregiver contact, and the limitations these restrictions place on task type (e.g., covert vs. explicit responses) and participant retention (Holland et al., 2007; Wood et al., 2004), limit application. Less invasive techniques with greater flexibility such as transcranial Doppler (TCD), which can measure cerebral blood flow velocity in the major cerebral arteries, are increasingly being used in the investigation of developmental origins and significance of language lateralisation (Bishop, Badcock, & Holt, 2010). So far in older children and adolescents, studies using a functional application of TCD recordings from the middle cerebral artery during picture or animation descriptions also show a predominant left lateralisation, and consistent with fMRI studies, no change in this pattern between the ages of 6–16 years (Groen et al., 2012; Haag et al., 2010). However, in the small number of studies available, there is disagreement as to whether such lateralised activation is associated with better language ability (Groen et al., 2012; Lohmann, Drager, Muller-Ehrenberg, Deppe, & Knecht, 2005).

In typically developing infants, near-infrared spectroscopy (NIRS), as well as TCD, have allowed for greater investigation of the developmental progression of language lateralisation. Using NIRS, Bortfeld, Fava, and Boas (2009) have shown greater hemodynamic activation in left temporal regions to an audio–visual presentation as opposed to visual only in 21 infants aged 6–9 months. Molavi et al. (2013) found a left-lateralised response to language in 19 newborn infants, and Peña et al. (2003) observed greater activation in left temporal areas in 12 newborns, 2–5 days post-birth, when exposed to normal speech compared to backward speech or silence, suggesting a lateralised response is already present at birth. FMRI data generally support these observations, showing that in 2-day-old newborns, language activation to speech is less lateralised compared to adults (Perani et al., 2011), but a left hemisphere advantage to speech over music is found in slightly older infants (Dehaene-Lambertz et al., 2010). To further test the idea of pre-birth development of lateralised response to language, bilateral brain response using NIRS to a familiar language (the primary language heard *in utero*) was greater compared to a decrease in activation to an unfamiliar language in 20 newborns within the first 3 days of birth (May, Byers-Heinlein, Gervain, & Werker, 2011). The neural processing of language therefore appears to be influenced by experience before birth.

Collectively, it appears that people are born with a preference for left lateralisation to language. However, this preference is strongly shaped by experience and begins to develop prior to birth and rapidly develops thereafter, remaining relatively stable throughout later childhood and possibly increasing further into adolescence and adulthood. What is missing from the literature and from a developmental perspective is analyses of lateralised response during the intermediary period between infancy and school-age. This is arguably the most difficult period in which to perform such studies from a compliance point of view, but is also the period of dramatic expressive language development. It would therefore seem a crucial period of life to examine lateralised response to language if we are to have a complete understanding of its origins and significance. Only a few studies have investigated such functions in preschool aged children, and all of these in clinical populations.

Sowman, Crain, Harrison, and Johnson (2014) investigated functional activation of brain regions using MEG to a picture naming task in 12 stuttering and 12 typically developing children aged 3–5 years. Their results show a predominant left activation in all children in language regions. In contrast to the more distributed or right language activation seen in adult stutterers (Brown, Ingham, Ingham, Laird, & Fox, 2005), these results suggest that at the time of pronounced expressive language development, and the typical emergence of stuttering, the pattern of brain activation is quite different and consistent with typically developing peers, supporting the maturational perspective on language and lateralisation development.

In contrast, Sato et al. (2011) used NIRS to assess lateralised responses to contrasts of phoneme (different vowels) and prosody (different vowel pitch) in a small group of 3- to 5-year-old children who stutter, and compared results to controls as well as to equivalent comparisons in 6- to 12-year-old children and adults. Consistent with the ideas put forward by Minagawa-Kawai et al. (2011), controls in each age group showed a predominant left side activation to phonemic contrasts compared to a more right side activation to prosodic contrasts. However, all stuttering groups showed a similar activation across both hemispheres for both conditions. While this result might seem at odds with Sowman et al. (2014), it is interesting to note that Sato et al. also showed a correlation between increased stuttering severity in adults and reduced lateralisation in the phonemic condition, an effect that was not found in either school- or preschool-aged children.

Most recently, Bishop, Holt, Whitehouse, and Groen (2014) investigated lateralised function to silent animation descriptions using fTCD in 57 4-year-old children with or without impaired language development. Children with language difficulties did not show left-side lateralised activation, compared to a clear left lateralisation in children without language problems. However, consistent with the observation in older children, while those with language impairment showed reduced left-lateralised activation, many 4-year-olds with right-lateralised activation showed no language difficulty. Combined, these few results from preschool populations support the argument that a more bilateral or right-lateralised response to language reflects adaptive neuroplastic changes, rather than represent an underlying cause of impairment. To date no study of functional language lateralisation exists in a purely typically developing group of preschool aged children. The aim of this study was to explore lateralised response to language in a relatively large group of typically developing young children, and to assess the association of both mean lateralised response and variability in response to language and broader cognitive development.

## 2. Material and methods

### 2.1. Participants

Participants with known visual or auditory impairments, diagnosed learning problems, developmental delays or syndromes affecting cognitive development (e.g., autism or downs syndrome) were excluded from the study; as were those currently taking medication known to affect cardiovascular blood vessel function or neurocognitive performance (such as a stimulant or psychotropic drug) or who were suffering from any acute illness, such