Biological Psychology 125 (2017) 173–176

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Short communication

# Measurement reliability of atypical language lateralisation assessed using functional transcranial Doppler ultrasound

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ARTICLE INFO

*Article history:*
Received 26 October 2016
Received in revised form 23 February 2017
Accepted 13 March 2017
Available online 16 March 2017

*Keywords:*
Transcranial doppler
Cerebral blood flow measurement
Speech
Hemispheric lateralisation
Reliability

ABSTRACT

It is well established that some individuals present with atypical, non-left hemisphere, cerebral lateralisation for language processing. However previous studies exploring the reliability of functional blood flow responses to detect lateralised activation during speech have focused only on individuals with typical left sided dominance. Here we report test-retest and between-task reliability measures obtained with functional transcranial Doppler ultrasound in 47 participants, including 9 with atypical language presentation. Results showed good test-retest reliability in atypically lateralised individuals, even after an interval of 120 days. Between-task reliability was weaker, but still within acceptable ranges.



## 1. Introduction

It is well established that the left cerebral hemisphere is dominant for language processing and production in the majority of people. However it is also known that some individuals have atypical hemispheric representation for speech processing, such that there is a deviation from the typical pattern of left hemisphere dominance (Deppe et al., 2000; Knecht, Deppe et al., 2000). This reduced left sided bias is observed more frequently in individuals who are left handed (Knecht, Dräger et al., 2000) and in some neurodevelopmental disorders such as Dyslexia (Illingworth & Bishop, 2009), Specific Language Impairment (Bishop, Holt, Whitehouse, & Groen, 2014) and Developmental Coordination Disorder (Hodgson & Hudson, 2016). However, little is known about why atypical language lateralisation occurs (see Bishop, 2013) and whether such lateralisation profiles are stable across tasks and between measurement sessions. Increased variability in lateralisation indices have been reported in people with atypical language representation (Knecht et al., 2003) as well as in young children (Kohler et al., 2015) and there is a suggestion that laterality profiles of individuals who display a reduced left hemisphere bias may be indicative of distributed cortical activation due to task complexity, rather than of altered language processing (Brownsett et al., 2014).

Here we report on the test-retest and between-task reliability of functional Transcranial Doppler (fTCD) for measuring hemispheric speech lateralisation, with a focus on the measurement reliability in individuals with atypically represented speech. fTCD is an ultrasound technology which uses a 2 MHz pulsed sound wave to insonate through areas of temporal bone in order to detect cerebral blood flow velocity (cBFV). Changes in velocities within the middle cerebral arteries can be examined during various cognitive tasks involving speech and language, motor action, perception and visuo spatial processing. Bi-modal recording allows simultaneous measurements to be taken from the left and right sides of the head, meaning the methodology provides a useful role in the cognitive neuroscience of hemispheric lateralisation. The advantages of fTCD are that the technology is quick to administer, very affordable (especially compared to other imaging techniques) and portable. fTCD is highly suitable for use with young children, patient groups and others not able to undergo more invasive or intimidating imaging procedures. As a research tool fTCD is becoming increasingly popular, helped by the recent advances in analysis software available (Badcock, Holt, Holden, & Bishop, 2012).

Previous reports indicate good reliability for measures of speech lateralisation using fTCD (Knecht et al., 1998; Stroobant & Vingerhoets, 2001), but it is less clear whether this is also the case for individuals who display atypical hemispheric lateralisation. Small sample sizes in previous studies on test re-test reliability (10 and 20 subjects respectively) mean it is difficult to draw conclusions about variance levels within atypical dominance, as none of the subjects in these studies had atypical speech representation. In contrast, between-task reliability for speech lateralisation

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http://dx.doi.org/10.1016/j.biopsycho.2017.03.008
0301-0511/

has been more widely assessed using fTCD (Bishop, Watt, & Papadatou-Pastou, 2009; Stroobant, Van Boxstael, & Vingerhoets, 2011) primarily with a view to ascertaining reliability of child-friendly paradigms designed to probe speech compared to standard verbal fluency tasks used with adults. But lateralisation profiles in these studies are often only reported at the group level, again meaning that judgements about individual variability are difficult to make.

## 2. Methods

We obtained language lateralisation indices using fTCD imaging during a word generation task (Knecht, Deppe et al., 2000) from 47 healthy adult participants (15 males; aged 18–59 yrs, mean age = 23.5 yrs; SD age = 8.4; 18 right handed and 29 left handed). Hand preference was determined by responses to a 21-item handedness inventory (Flowers & Hudson, 2013), from which handedness quotients were derived using the following formula: (Right − Left)/(Right + Left) *100. Scores above 0 denoted right handedness and scores below 0 denoted left handedness. We deliberately targeted left handed individuals to increase the likelihood of atypical language representation in our sample. The same 47 participants returned to the lab to undergo a second session of fTCD imaging during the same word generation task between 59 and 121 days after session 1 (mean separation was 81 days, SD: 18.2). For 33 of the participants (11 males; mean age = 22.1 yrs; SD age = 5.3; 11 right handed and 22 left handed) lateralisation indices from a second speech production paradigm, animation description (Bishop et al., 2009) were also obtained during session 1, allowing for a within subjects comparison of task reliability. The reduction in sample size is due to variability in the set-up time between participants, meaning in 15 cases there wasn't time to run the second speech paradigm. Ethical approval for the work was obtained from University of Lincoln School of Psychology, and all participants gave informed consent. None had neurological or cerebrovascular disorders, or impairments with language or reading; all had normal or corrected to normal vision.

### *2.1. Speech paradigms*

#### *2.1.1. Word generation*

This task involves participants generating words to a single letter cue. Each trial began with a 5 s period in which participants were prompted to clear their mind. A letter was then presented in the centre of the computer screen for 15 s, during which time participants were required to silently generate as many words as possible that began with the letter displayed. (At the onset of the trial a 500 ms epoch marker was simultaneously sent to the transcranial Doppler). Following the generation phase, to ensure task compliance, participants were requested to report the words aloud within a 5 s period. The trial concluded with a 35 s period of relaxation to allow CBFV to return to baseline before the onset of the next trial. The WG paradigm consisted of 23 trials in total. Letter presentation was randomised and no letter was presented more than once to any given participant. The letters 'Q', 'X' and 'Y' were excluded from the task. Within fTCD ultrasound research word generation has been used extensively (Bishop et al., 2009; Knecht, Deppe et al., 2000; Knecht, Dräger et al., 2000) and is widely considered to be a reliable paradigm for determining language dominance in this technique (Knecht et al., 1998).

#### *2.1.2. Animation description*

this task was developed from the desire to test pre-literate children on speech production tasks (Bishop et al., 2009), in order to answer questions about the developmental trajectory of hemispheric language lateralisation. The paradigm, (described in detail by Bishop, Badcock, & Holt, 2010), requires participants to watch a 12 s cartoon in silence, and then to report what they had seen in the clip at the onset of a question mark 'speak' prompt. This 'speak' phase lasts for 10 s, which is then followed by a rest phase for 8 s to allow the CBFV signal to return to baseline. The baseline period is taken from the 'watch' phase of the paradigm. Each trial lasts 30 s and there are a total of 20 animation clips displayed, in a random order generated by a python based computer script.

#### *2.1.3. fTCD analysis*

Relative changes in cBFV within the left and right Middle Cerebral Arteries (MCAs) were assessed using bilateral fTCD monitoring from a commercially available system (DWL Doppler-Box$^{TM}$X: manufacturer, DWL Compumedics Germany GmbH). A 2-MHz transducer probe attached to an adjustable headset was positioned over each temporal acoustic window bilaterally. PsychoPy Software (Peirce, 2007) controlled the speech production paradigms and sent marker pulses to the Doppler system to denote the onset of a trial. Data were analysed off-line with a MATLAB (Mathworks Inc., Sherborn, MA, USA) based software package called dopOSCCI (see Badcock et al., 2012 for a detailed description). Data processing and analysis for the Animation description paradigm was undertaken as per Hodgson, Hirst, and Hudson (2016) and the word generation paradigm was analysed as outlined in Hodgson and Hudson (2016).

Speech laterality indices were derived for each participant based on the difference between left and right sided activity within a 2 s window, when compared to a baseline rest period of 10 s. The activation window was centralised to the time point at which the left-right deviation was greatest within the period of interest (POI) (Badcock et al., 2012). In the word generation paradigm the POI ranged from 3 to 13 s following presentation of the stimulus letter. For the animation description task the POI ranged from 12 to 22 s following onset of the trial. Speech laterality was assumed to be clear in all cases in which the LI deviated by > 2 SE from 0. Left-hemisphere or right-hemisphere speech dominance was indicated by positive or negative indices respectively. Cases with an LI <2 SE from 0 were categorised as having bilateral speech representation. Individuals were categorised as having 'Typical' speech representation if they displayed a clear LI score which was positive, alternatively individuals with a bilateral LI score *or* a clear LI score which was negative were categorised as having 'Atypical' speech representation (Flowers & Hudson, 2013; Hodgson et al., 2016). Participants required a minimum of 75% acceptable trials to be included in the analysis; all participants reached this threshold.

## 3. Results

LI scores from the word generation paradigm resulted in 9 individuals classified as atypically lateralised (displaying either right sided activation or activation less than 2 SE from 0; LI scores ranged from −4.43 to 0.81) and the remaining 38 individuals with typical left hemisphere lateralisation (LI scores ranged from 1.19 to 6.61). LI scores from Time 1 (T1) and Time 2 (T2) on the word generation task revealed a strong positive correlation, $r(47) = 0.79$ $p = 0.0001$, indicating that fTCD has a good test re-test reliability even after a delay in re-testing of over 120 days (see Fig. 1a). During this task 8 individuals with atypical speech laterality at T1 all replicated an atypical lateralisation profile at T2. One individual shifted from a bi-lateral profile at T1 to a right sided bias at T2.

To assess the comparability, rather than just the relationship, between the two measurements taken, a Bland-Altman (B-A) analysis (Altman & Bland, 1983) was conducted. This is a method of quantifying agreement between two quantitative measurements by constructing limits of agreement. These statistical limits are calculated by using the mean and the standard deviations of the