What Box: a task for assessing language lateralisation in young children

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Abstract

The assessment of active language lateralisation in infants and toddlers is challenging. It requires an imaging tool that is unintimidating, quick to setup, and robust to movement, in addition to an engaging and cognitively simple procedure that elicits language processing. Functional Transcranial Doppler Ultrasound (fTCD) offers a suitable technique and here we report on a suitable method to elicit active language production in young children. The 34-second 'What Box' trial presents an animated face 'searching' for an object. The face 'finds' a box that opens to reveal an object, which may be labelled spontaneously, in response to a "What's this?" prompt, or in response to the object label. What Box conducted with 95 children (1 to 5 years-of-age, completing a median of 7 trials), who were left-lateralised on average. The task was validated (ρ = 0.4) against the gold standard Word Generation task in a group of older adults (n = 65, 60 to 85 years-of-age, median of 24 trials). Existing methods for assessing lateralisation of active language production have been used with 4-year-old children while passive listening has been conducted with sleeping 6-month-olds. This is the first active method to be successfully employed with infants, toddlers, and pre-schoolers, and show good correspondence to Word Generation in older adults.

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Introduction

The specialisation of cognitive capacities to the left and right cerebral hemispheres is referred to as the lateralisation of cognitive function and, in most people, the left hemisphere is specialised (or dominant) for language processing whilst the right is specialised for visuo-spatial processing. There is evidence that this specialisation for language reception is apparent early in development (Dehaene-Lambertz, 2000) but the lateralisation of language production has been harder to determine. Here we report a method for examining language reception and production that is suitable for use with young children.

Owing to the inherent difficulty for children below the age of 5 to stay still – a significant problem for functional Magnetic Resonance Imaging (fMRI) – researchers have favoured functional Transcranial Doppler Ultrasound (fTCD) for investigating language lateralisation in this age group. FTCD is used to measure the blood flow velocity in the left and right cerebral arteries, most commonly, the middle cerebral arteries (Aaslid, Markwalder, & Nornes, 1982; Newell & Aaslid, 1992); faster event-related velocities in a given hemisphere are indicative of cerebral lateralisation for that event (i.e., language production). The gold standard task for assessing language lateralisation using fTCD is Word Generation task. It involves the generation of words beginning with a visually presented letter (Knecht et al., 1996). The task is reliable (Knecht, Deppe, Ringelstein, et al., 1998; Stroobant & Vingerhoets, 2001), and has been validated against Wada (Knake et al., 2003; Knecht, Deppe, Ebner, et al., 1998) and fMRI (Knecht, Deppe, Ebner, et al., 1998; Somers, Neggers, Kahn, & Sommer, 2011). However, whilst Word Generation works well for adults, silent word production to a letters and long periods of relaxation are not suitable for children. Fortunately a number of more appropriate tasks exist.

Child-friendly fTCD tasks include Picture Description (Haag et al., 2010; Lohmann, Drager, Muller-Ehrenberg, Deppe, & Knecht, 2005), Animation Description (Bishop, Watt, & Papadatou-Pastou, 2009), and Story Listening (Stroobant, Van Boxstael, & Vingerhoets, 2011). These tasks have been used with children as young as four-years-of-age but continue to rely on sustained periods of rest and attention. Picture Description and Story Listening require 30 seconds of rest followed by 30 seconds of production or listening. The animation description task is more child-friendly with 12 seconds of animation following by 10 seconds of production and 8 seconds of rest. However, the reliance on overt production and 8 seconds of rest are difficult for children below the age of four.

Covert language have been used successfully to activate the cerebral structures involved in overt production (Bookheimer et al., 1998). Furthermore, the strength of lateralisation is considered similar for covert and overt production (Gutierrez-Sigut, Payne, & MacSweeney, 2015). Taking advantage of this, Wilke et al. (2005) developed tasks that induce the automatic covert production of predictable words that are replaced within sentences by a tone. For example, “A frog lived under a flower. One day a girl picked the [tone].” Observers automatically fill-in the missing word as evidenced by increased functional activity in areas usually associated with overt production. This activity is enhanced by the presentation of a picture of the missing word. This covert production task has been successful with children as young as six-years-of-age using fMRI (Lidzba, Schwilling, Grodd, Krägeloh-Mann, & Wilke, 2011). Using fTCD, this task has been compared with Word Generation in adults but lateralisation was weaker and less reliable than Word Generation (Badcock, Nye, & Bishop, 2012). However, participants were not given instructions and the paradigm did not explicitly encourage labelling.

The other concern with the use of fTCD with children is maintaining task interest during periods of rest, when blood flow velocity returns to a resting state (see Deppe, Ringelstein, & Knecht, 2004). This is 40 secs for Word Generation, during which participants are asked to relax and think of nothing. For the Animation Description task, the period is significantly reduced to 8 secs and includes an image of a boy in a 'Shh' gesture (Bishop et al., 2009), however, our pilot work determined that this task was not suitable to maintain 18-month-olds' interest.

The What Box Task

The 'What Box' task follows from this literature as a procedure to elicit covert or overt language production in young children. Very simply, the task includes a line drawing of a face 'searching' for a box. Upon 'finding' the box, an image of an object is presented and children are encouraged to label this object. Here we build upon a previous report of the task (Kohler et al., 2015), providing a detailed methodology for the presentation and administration of the task as well as updated processing and analysis techniques for use with fTCD in young children (Experiment 1) and older adults (Experiment 2). Experiment 2 also includes a novel validation of What Box with the Word Generation task.

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Experiment 1, methodology in young children: Materials and Methods

Participants

Participants were 95 children between 1- and 5-years-of-age. Children were included if English was the primary language, they had no known visual or auditory impairments, learning problems, developmental delays or syndromes affecting cognitive development (e.g., autism or Down syndrome), they were not currently taking medication known to affect cardiovascular blood vessel function or neurocognitive performance (such as a stimulant or psychotropic drug) or suffering from any acute illness, such as a cold.

The mean age of included children was 39.46 months (SD = 15, min = 12, max = 67), born between 35-42 weeks gestation, and 49 (52%) were male. In addition to age and gender, child ethnicity (90% Caucasian) and socioeconomic status (1009.2 ± 47.9; using the Australian Bureau of Statistics Index of Relative Socio-economic Advantage/Disadvantage 2011 national census data (National mean = 1000, SD = 100) were recorded. Hand preference was determined by planned observation of the use of age-appropriate objects, based on methods used in children from 6-months of age (Michel, Ovrut, & Harkins, 1985): 76 (80%) were right-handed, 12 (12.63%) were left-handed, and 7 (7.37%) did not demonstrate a dominant hand.

Procedure

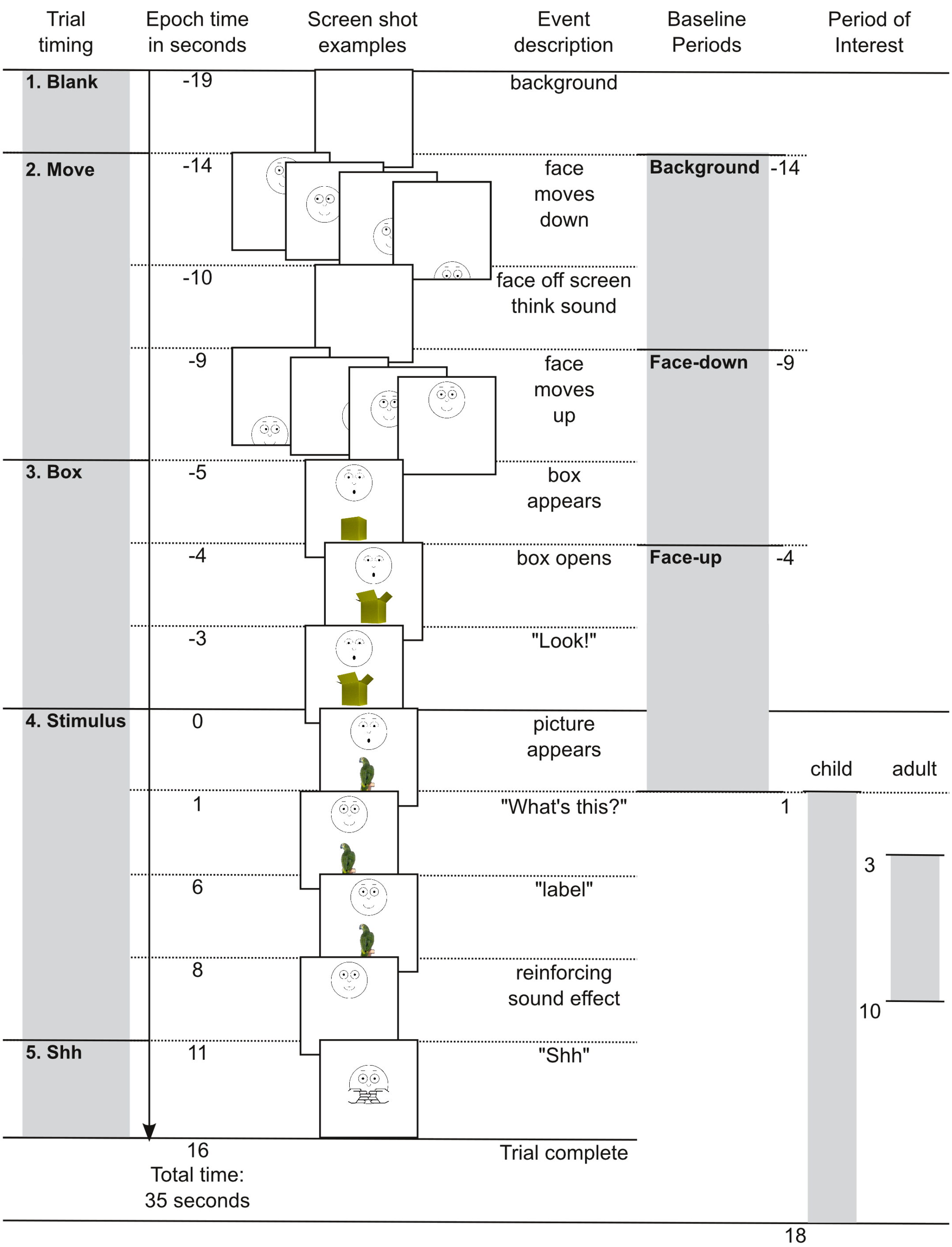
What Box

The What Box task includes an animation of a face 'searching' for an object. The animation is created with a series of still-frame images and accompanying sounds (see Figure 1 for a schematic diagram of a trial). The key steps are:

1. the face 'moves' down and then up the screen
2. a box appears then opens followed by a spoken "Look!"
3. the box is then replaced by an object and a spoken "What's this?"
4. the object's verbal label is presented after a delay to allow for verbal labelling
5. a face with hands covering its mouth appears with the spoken "Shh"

The visual stimuli include backgrounds, faces, boxes, and objects. The backgrounds were coloured photographs including houses, rooms (e.g., kitchen, bedroom), and natural scenes (e.g., gardens, landscapes). Images were blurred and mirrored: blurring reduced the presence of attention-capturing, high-contrast features and mirroring (along the vertical centre) controlled for any bias in the lateralisation of visual attention between hemifields. Some of these images did contain nameable objects, however, the degradation of the images and context meant that we did not observe evidence of overt or covert labelling to these backgrounds. The faces were blue in colour, included two eyes and eyebrows, a nose, and a mouth. Black pupils were set in white eyes and pupil position was varied to adjust gaze direction (centred, up, down, left, or right). Eye-shape was altered from full circles to horizontal crescents to indicate surprise (see 'box appears' event in Figure 1). The mouth shape included a u-shaped line smile; a vertically oriented, black oval to indicate surprise; and a horizontal u-shaped, white crescent 'smile' as reinforcement for monitoring the display. Images of open and shut cardboard boxes were presented in 14 different colours (aqua, light and dark blue, brown, light and dark green, orange, pink, purple, red, rust, turquoise, white, and yellow). There were 33 different images of objects (e.g., biscuit, bottle, and animals, for a full list see Supplementary Table 1) selected as items commonly known by 18-month-old children (from the Oxford Study of Children's Communication Impairments databases).

The auditory stimuli included: spoken labels for each of the objects, "Look!" recorded with rising intonation to capture attention, "What's this?", and a series of sound-effects: 13 action files (e.g., spring, cork pop, or whistle), 3 to indicate 'thinking' (e.g., Hmm), and 26 celebratory sounds used for reinforcement (e.g., crowd cheers, "yahoo", "yay", and laughing). The spoken words were recorded in a female British accent.



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166 Figure 1. A schematic diagram of a What Box trial. Includes trial timing, event
167 descriptions, and baseline and period of interest timings for children and adult
168 data processing.

Trial timing

Each trial lasted 35 seconds. The timings will be described in 5 periods relative to the animation, including the duration of the period and the timing relative to the presentation of the object at time 0 (for a diagram see Figure 1).

1. Blank (5 sec, -19 to -14): A randomly selected background was presented for 5 sec then remained as the background until the object appeared (i.e., time 0).
2. Move (9 sec, -14 to -5): The face stimulus was presented at locations simulating movements down then up the screen. The location changed at 1 sec intervals and was accompanied by a randomly selected action sound. There were four down and four up vertical locations randomly varied to be within the four vertical quarters of the screen. The horizontal positions were varied to left or right of centre within a corridor 20% of the screen width. This corridor was used to avoid any bias in the lateralisation of visual attention. The position of the eyes also varied randomly at each position (i.e., looking left, right, up, and down) except for the top position of the screen when they were straight ahead (i.e., looking at the participant). Following the downward movement, the face ‘moved’ off the bottom of the screen for 1 sec, accompanied by a ‘thinking’ sound. Following the upward movement, the face always finished horizontally centred in the top quarter of the screen.
3. Box (5 sec, -5 to 0): A box was presented and opened with an action sound at each step, 1 sec between each step, and the face looked down

and surprised. The “Look!” cue was then presented to direct attention to the screen, 3 sec.

4. Stimulus (11 sec, 0 to 11): The object was presented on a black background (the face remained in the top central position looking surprised and straight ahead at the participant), for 1 sec during which an event marker was sent for data analysis. The “What’s this?” cue was then played. After 5 secs (allowing for word generation/production) the object auditory label was played. After 2 sec a smiling face, with a reinforcing sound effect, was presented and remained on screen for 3 secs. The objects were presented in alphabetical order.
5. Shh (5 sec, 11 to 16): A larger face with hands over its mouth was then presented for 5 sec accompanied by a ‘Shh’ sound.

Functional Transcranial Doppler Ultrasonography

We used a Doppler ultrasonography device (Doppler-Box™, DWL Elektronische Systeme, Singen, Germany) with an adhesive conductive gel (Tensive® by Parker) or Echoson® Ultrasonographic Gel (Sonogel Vertriebs GmbH) to examine the blood-flow velocity through the left and right middle cerebral arteries (MCAs). The choice of gel depended on the age and compliance of the child: the adhesive gel being used with younger and less compliant children as it can be placed on the temporal window without running which is more convenient for setup. Participants were fitted with a Diamon® headset or elastic headbands that held in place a 2-MHz transducer probe over each temporal skull window. Participants were seated at a viewing distance of approximately 50 cm from a computer screen. The task was presented using a

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personal computer with a 22-inch Dell P2210 monitor. The procedures were programmed using MATLAB R2011b (Mathworks, Natick, MA, USA) that sent parallel port pulses as event markers (we used the io32.dll from http://apps.usd.edu/coglab/psyc770/IO32.html).

Testing Session

The data were collected as part of ongoing research at the University of South Australia, Cognitive Neuroscience Laboratory. The research was approved by the University of South Australia and the Women's and Children's Health Network Human Research Ethics Committees (reference: 0000025883 & REC2288/6/13 respectively) and guardian's provided informed written consent for their child's involvement in the research. Preliminary findings have been reported elsewhere (Kohler et al., 2015). Following standardised test administration, each child was familiarised with the TCD headset. This included demonstrating the equipment on one of the two or three researchers present as well as the parent, and allowing the child to play with and decorate the headset with stickers. If necessary a teddy bear 'helper' was fitted with the headset and read the book 'I can hear my brain' with the child (see supplementary materials). Children sat on a chair or on their caregivers lap (younger, < 3, and non-compliant children), watching a favourite television programme, while the headset or headband was then fixed in place and probes attached. The headset was a better fit for older children, while the headbands were more suitable for younger children or those with asymmetric heads. Upon the accurate detection of the MCA (confirmed by bifurcation checking when possible) on the left and right side, the probes were fixed in place.

We recommend the following steps for optimal insonation:

1. Brush hair backwards and out of the way
2. Ask the child to yawn whilst looking at the temple – this can give a good indication of the 'dint' or thinnest part of the skull.
3. Begin searching for the MCA at the following location: making reference to the outer canthus of the eye, move posteriorly to the hairline, to above the zygomatic arch.
4. Position the probe to be facing slightly upwards and forwards, towards the back of the contralateral eye.
5. Using small steps, move the probe around an imaginary clock-face to find the best point of insonation.
6. Increase software gain and reference the M-Mode spectrograph to determine optimal depth and position.
7. Increase the depth of the pulse to find the MCA bifurcation (indicated by bi-directional flow in the spectrograph) and reduce depth until the M1 section of the MCA is reached. This is where the cleanest signal should be found.

The task was introduced as a game with the aim of naming objects in a box that a face finds. The instructions were delivered in developmentally appropriate language including: i) the requirement to wait until something comes out of the box and ii) to label the object that comes out of the box. The first trial was used as practice to ensure the participant understood the requirements of the task. If necessary, the participant's attention was re-directed to the task throughout testing, and any gross motor movements or diversion from the task was recorded for manual epoch exclusion.

Data processing

The fTCD data was analysed using dopOSCCI (Badcock, Holt, Holden, & Bishop, 2012) version 3.0, a MATLAB-based summary-suite for fTCD data (see https://github.com/nicalbee/dopStep) . The data were trimmed to exclude irrelevant recording before the first and after the final epoch. Heart cycle artefacts were removed (see Deppe, Knecht, Henningsen, & Ringelstein, 1997; Deppe, Knecht, Lohmann, & Ringelstein, 2004) and smoothed using the 'linspace' MATLAB function between cycles. To remove dropout and spike artefacts, values beyond -3 or 4 standard deviations from the mean, affecting less than 5% of the data, were adjusted using 'linspace' between values 1.5 secs either side of the extreme value (see Table 1 for descriptive statistics related to these atefacts). This step was conducted using the dopOSCCI dopActCorrect function and is based on the suggestion from Dorothy Bishop (personal communication). The data were epoched from baseline onset (see below) to 18 secs relative to event markers, and normalised to a mean of 100 within each epoch (i.e., not overall), correcting for left and right probe angle differences (see Deppe, Knecht, et al., 2004).

Table 1

Median, interquartile range (IQR), maximum, and the number of datasets adjusted (n adjusted) by the activation correction procedure.

Channel	Direction	Median	IQR	Maximum	n adjusted
left	< - 3 SD	0	3.54	100	24
	> 4 SD	0	0	0.73	1
right	< - 3 SD	0	13.52	100	32
	> 4 SD	0	0	3.81	2

Epochs with extreme values were excluded: values beyond ± 50% of the mean or with a left-minus-right difference greater than 8% affecting more than 1% of the data within the epoch. Regarding activation separation, we know that the desired effects will be in the magnitude of 3 to 5% change at most, therefore, separations greater than this are likely due to artefact. The cut-off of 8% was based on the 60th percentile (8.12) of the median difference of the sample (average median difference was 6.6%, interquartile range = 11.39%). We examined the split-half reliability (correlation between laterality indices calculated for the odd and even epochs) as a function of the minimum number of epochs included in the calculation at separations of 7 and 10 (55th and 65th percentiles respectively), and with no screening. The number of available epochs varied between individuals and depended upon the activation separation screening. Without screening, the reliability was poor. At an 8% cut-off, the reliability was strongest (see Figure 2). Second-order quadratic equations ($y = B_0 + B_1x + B_2x^2$) differentiated the 8% and 7% separation from the 10%; $F(6,18) = 4.46$, $p < .001$ (no screening was not included in the analysis); with R^2 values of .99, .84, and .49 respectively (see Table 2 for parameter statistics). The same curve adequately fitted the 8% and 7% separations, $F(3,12) = 1.02$, $p < .42$. We used the more inclusive cut-off: 8%. These summaries at based on a -4 to 1 baseline period.

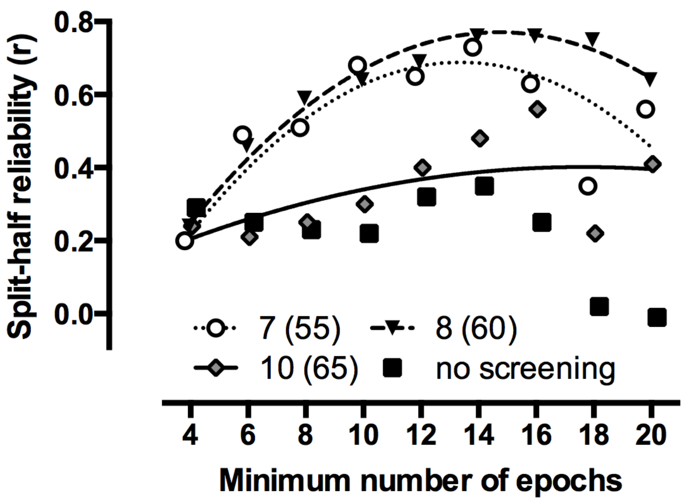

Figure 2. Split-half reliability (Pearson product moment r values) for four levels of left-minus-right activation separation (7, 8, 10, and no screening, numbers reflecting the 55th, 60th, and 65th percentiles of the median difference of the sample respectively) as a function of the minimum number of epochs included in the calculation. The best fitting quadratic regression lines are displayed for separations of 7 (dotted line), 8 (dashed line), and 10 (solid line).

Table 2

Second-order polynomial parameter statistics for activation separation cut-offs as a function of the minimum number of epochs included in the calculation.

Separation % (%ile)	Parameter		
	B0	B1	B2
7 (55)	-0.26 [-0.6 0.07]	0.14 [0.06 0.22]	-0.005 [-0.009 -0.002]
8 (60)	-0.21 [-0.31 -0.12]	0.13 [0.11 0.16]	-0.005 [-0.006 -0.004]
10 (65)	0.07 [-0.28 0.43]	0.04 [-0.04 0.11]	-0.001 [-0.004 0.002]

Epochs were also excluded manually (using dopOSCCCI: dopEpochScreenManual function). Manual exclusion was applied to epochs if the participant was observed to be disengaged from the task, conducted gross movements, or was talking during the baseline period. The median number of manually excluded epochs was 2 (IQR = 6, min = 0, max = 20).

As this is a new paradigm, we tested three baseline periods to determine the most suitable, using split-half reliability as an index of quality, bearing in mind the 5 to 7 sec delay due to the timing of neurovascular coupling (Malonek et al., 1997; Rosengarten, Osthaus, & Kaps, 2002). The three baseline periods were:

1) 'background', -14 to -9 secs, including activity to the presentation of the background, commencing 10 secs after the onset of 'Shh';

2) 'face-down', -9 to -4 secs, including activity to the presentation of the face moving down the screen, commencing 10 secs after the onset of the background; and

3) 'face-up', -4 to 1 secs, including activity to the presentation of the face moving up the screen, commencing 10 secs after the onset of the face.

The baseline periods are displayed in Figure 1. Baseline correction was conducted, subtracting the mean of data within the baseline period from all other data points.

Laterality Indices (LIs) were calculated as the average left minus right signal over a 2 sec period surrounding the peak left-right difference within the period of interest: 5 to 18 secs. Positive LI values indicate left lateralisation, negative indicate right.

To determine whether the LI was significantly different to zero, a one-sample t-test was applied to the LI values for the group. Split-half reliability was calculated based upon LIs calculated for the odd and even numbered epochs, adjusted to equate the number of odd and even epochs used.

Data recording error

Eight of the recordings were affected by an incorrect software setting that set an upper-limit on the recorded velocity: blood-flow velocities above 133 cm/secs were saved as 133 (automatically detected as > 2% of the signal being equal to the maximum value, see dopOSCCI 'dopClipCheck' function for more information). In order to determine whether this significantly affected the LI calculations, this limit was artificially set for the processing of the all other data sets. The percentage of artificially clipped data ranged from 0.01 to 36% with a mean of 11.77%. The LI calculations were not affected; mean difference = -0.19 (SD = 1.79), $t(138) = -0.38$, $p = 0.70$; and showed a strong correspondence, $r = 0.82$, $p < .001$. Therefore, the restricted data were included in the full analysis. These summaries at based on a -4 to 1 baseline period.

Results

The group-averaged change in blood flow velocity, for the left and right MCAs, relative to object presentation is displayed in Figure 3. There are three features to note. The first feature is an early (around 3 secs), non-lateralised peak that likely reflects a rapid, attention-related response to the object presentation. The second feature includes two, left-lateralised peaks (around 6.5 and 16 secs) that likely reflect a labelling response to the object and a receptive or repetition response to the verbally presented label. These peaks are included in the period of interest. The third feature is convergence of the left and right velocities: evident at 22 seconds. This has implications for the selection of the baseline period. The continuation of task-related activity into the 'Blank' phase of the next trial (see Figure 1) has an impact on the task reliability, dependent upon the timing of the baseline period; i.e., this continuation produces poorer reliability for the -14 to -9 baseline compared to -4 to 1 that does not have this continuation.

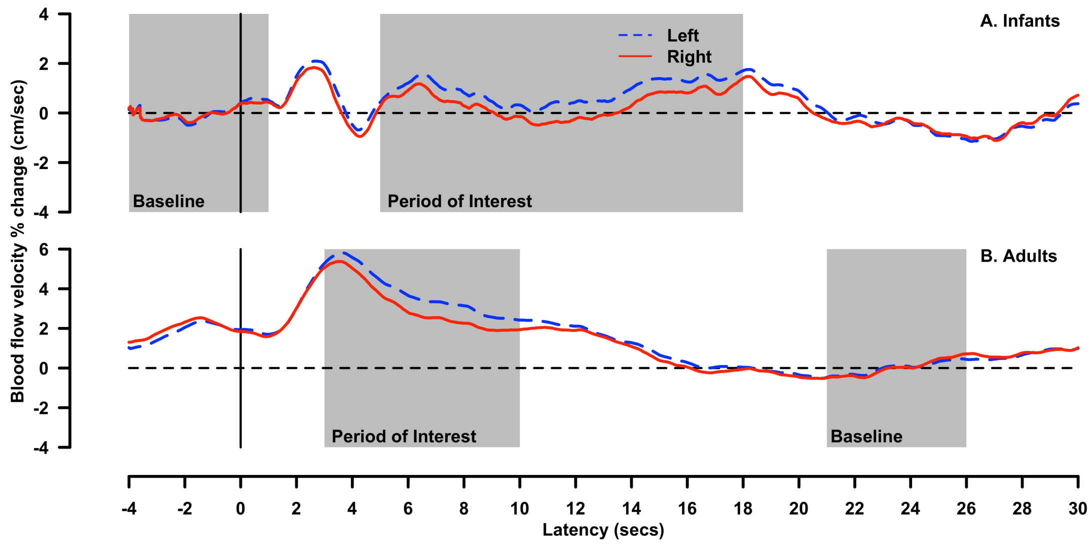

Figure 3. Group-averaged change in blood flow velocity relative to object presentation (Latency = 0 seconds) for the left (broken blue line) and right (solid red line) as a function of time (in seconds). Panel A displays the infant data (n = 79) that were calculated using a -4 to 1 sec baseline period (first grey panel). Panel B displays the adult data (n = 66) that were calculated with a 21 to 26 sec baseline (equivalent to -14 to -9 but adjusted for visualisation here to maintain the same x-axis). The periods of interest (-5 to 18 secs for infants and 3 to 10 for adults) are also displayed for reference. Please note the y-axis range is greater in panel B.

Split-half reliabilities were calculated for the three baseline periods for a range of epochs: 2 to 10 for odd and even epoch halves (i.e., at least 4 to 20 acceptable epochs in total). These reliabilities are displayed in Figure 4 (for a complete set of the summary statistics for these divisions including sample size, LI estimates, and reliability confidence intervals, see Supplementary Table 2). Second-order quadratic equations ($y = B_0 + B_1x + B_2x^2$, see Table 3 for best fitting parameter statistics, conducted with GraphPad Prism 6.0f) were fitted to the reliabilities to evaluate the relative suitability of the baseline periods. The reliabilities were higher and more consistent for the 'face-up' baseline: best fitting values differentiated the 'face-up' and 'face-down'; $F(3, 12) = 7.42$, $p < 0.01$. The following summaries are based on the -4 to 1 baseline period. In addition to reliability, this baseline retained a greater number of epochs across participants; likely due to shorter epoch duration, and fewer epochs rejected for artefacts (see the Data processing section for epoch rejection criteria).

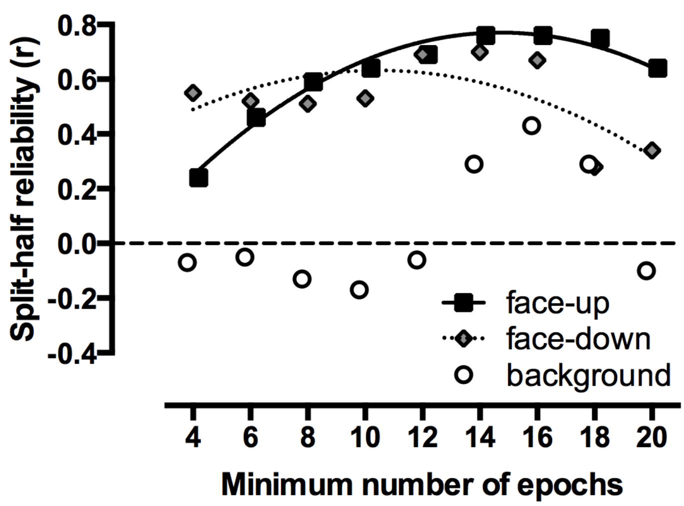

Figure 4. Split-half reliability (Pearson product moment r values) for three baseline periods (background = -14 to -9, face-down = -9 to -4, and face-up = -4

to 1) as a function of the minimum number of epochs included in the calculation. The best fitting quadratic regression lines are displayed for face-down (dotted line) and face-up (solid line) data.

Table 3

Second-order polynomial (quadratic) best fitting parameters, 95% confidence intervals, and R^2 values for reliability coefficients calculated for incremental numbers of epochs for two baseline periods.

Baseline	Parameters			
	B_0	B_1	B_2	R^2
-9 to -4	0.26 [-0.28 0.79]	0.07 [-0.03 0.17]	-0.003 [-0.007 0]	0.6
-4 to 1	-0.21 [-0.31 -0.12]	0.13 [0.11 0.16]	-0.005 [-0.006 -0.004]	0.99

There were 1 or more acceptable epochs for 77 participants: median = 7, IQR = 10, min = 1, max = 32. The distribution of all laterality indices (LIs) is displayed in Figure 5, panel A. The number of accepted epochs was weakly correlated with age such that older children had more accepted epochs, Spearman's $\rho = 0.38$ [0.18 0.59], $p < .01$.

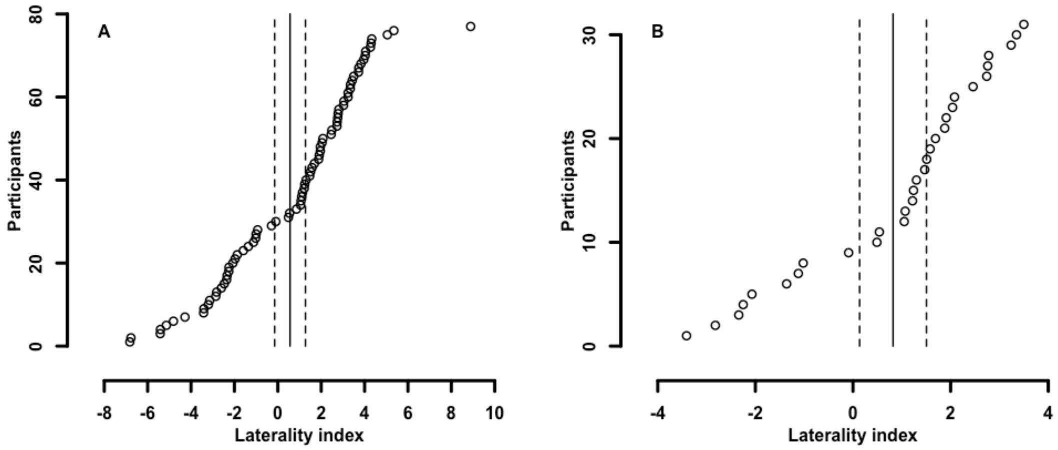

Figure 5. The distribution of laterality indices for A) participants with 1 or more accepted epochs (n = 77) and B) participants with 10 or more accepted epochs (n = 31). Sample mean (solid vertical line) and 95% confidence intervals (dashed vertical lines) are also displayed.

The minimum number of acceptable epochs for LI calculations varies in the literature from 8 (Gutierrez-Sigut et al., 2015) to 12 (Groen, Whitehouse, Badcock, & Bishop, 2011): here we used 10. Based on this criterion, the distribution of LIs for participants with 10 or more epochs is displayed in Figure 5, panel B. The number of accepted epochs (median = 14, IQR = 6, min = 10, max = 32) was not significantly related to age, Spearman's ρ = 0.06 [-0.32 0.45], *p* = 0.75. The mean LI was 0.82 (SD = 1.95, min = -3.41, max = 3.5, 95%CI = 0.68), which is statistically different to zero $t(30) = 2.35$, $p = 0.026$; and represents a medium effect size, Cohen's d = 0.42. On average, the group was left-dominant for language processing. The split-half reliability is 0.64 [0.37 0.81], $t(29) = 4.47$, $p < .001$.

Experiment 2, Validation in older adults: Materials and Methods

Participants

Participants were 67 adults with a mean age of 68.94 years (SD = 6, min = 60, max = 85), and 28 (42%) were male. All were right-handed as assessed using the Flinders Handedness Survey (Nicholls, Thomas, Loetscher, & Grimshaw, 2013).

Procedure

What Box

What Box was as described in Part 1, with the exception that a different set of stimuli was used and the task was discontinued after 20 trials with a correct response. There were 51 stimuli, chosen from http://websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.htm (for a list see Supplementary Table 1). There was a minimum of 25 trials, and 37 were required for two individuals to achieve 20 correct labels.

Word Generation

The Word Generation task was based on Knecht et al. (1996). There were 24, 60 sec trials corresponding with the letters of the alphabet, excluding ‘x’ and ‘z’. Each trial consisted of six periods (note: words in inverted commas were displayed on the screen and acted as instructions): 1. ‘Relax’ (20 sec), 2. ‘Clear Mind’ (5 secs), 3. a single, randomly selected letter was presented on the screen (2.5 sec), 4. silent word generation of words beginning with the presented letter (12.5 secs), 5. ‘Say’ (5 secs), 6. a blank normalisation period (15 secs). Brief

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auditory tones were presented at the start of the clear mind, say, and relax periods.

Testing Session

The data were collected as part of ongoing research at the University of South Australia, Cognitive Neuroscience Laboratory. The research was approved by the University of South Australia Human Research Ethics Committee (reference: 0000031040) and participants provided informed written consent for their involvement in the research. Findings for Word Generation have been reported elsewhere (Keage et al., 2015).

Data processing

What Box.

The What Box data were processed as described in Experiment 1 with the exceptions of timings and epoch exclusion by activation separation. The timings were: epoch -14 to 10 secs, baseline -14 to -9, and period of interest 3 to 10. As evidenced by the physiological response (see Figure 3, Panel B), the adults adhered to the instruction better than the children, requiring alternate timing. The baseline period was earlier, corresponding to 10 seconds after the 'Shh' instruction (see Figure 1 trial schematic). The period of interest was earlier and shorter, longer periods picked up a second component in some individuals resulting in changes from typical to atypical lateralisation and poorer internal reliability.

Epoch exclusion by activation separation was based on individually calculated cut-offs. The distribution of separations was smaller for adults than children – average median = 3.01 (IQR = 1.59, Min = 0.97, Max = 9.81) – indicative of less noise in the recordings. The median activation separation plus eight times the interquartile range was most reliable method of screening epochs for activation separation, increasing the split-half reliability from ρ = .65 [.45 .78] without screening to ρ = .71 [.52 .84]. Spearman's rank order correlations were used to reduce the impact of extreme values.

Word Generation.

The Word Generation data were processed as described in section 0 with timings based on previous research (Keage et al., 2015; Knecht, Deppe, Ringelstein, et al., 1998; Knecht et al., 1996); epoch -15 to 25 secs, baseline -15 to -5, and period of interest 5 to 15. Individually calculated cut-offs were used for activation separation epoch exclusion, fives times the inter-quartile range (for reference, the average median activation separation was 3.8, IQR = 2.89, Min = 1.16, Max = 13.06). This cut-off increased the split-half reliability from ρ = .77 [.63 .86] without screening to ρ = .82 [.69 .89].

Data Analysis

Data from participants with 10 or more accepted epochs for both What Box and Word Generation were included in the data analysis. Internal reliability was calculated using split-half Spearman rank-order correlations to minimise the influence of individuals with extreme LI calculations. Validity was calculated by disattenuating (Schumacker & Muchinsky, 1996; Spearman, 1904) the correlations between the LIs for the two tasks.

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Results

There were 65 participants with 10 or more epochs for both the What Box and Word Generation tasks (What Box: median = 24, IQR = 3, min = 15, max = 27; Word Generation: median = 22, IQR = 3, min = 11, max = 24). The mean LI for both tasks indicated left lateralisation overall: What Box = 0.95 (SD = 2.36, latency = 6.39, latency SD = 2.37), Word Generation = 1.57 (SD =2.47, latency = 9.31, latency SD = 2.75). The internal reliability for both tasks was high (What Box, $\rho = 0.71$, Word Generation, $\rho = 0.82$) and the disattenuated correlation between the two tasks was $\rho = 0.40$, indicating a medium correspondence between the two tasks. A scatter plot of the LIs for the two tasks is presented in Figure 6. As Word Generation is the gold standard fTCD task for the assessment of language lateralisation, we conclude that What Box also reflects language processing.

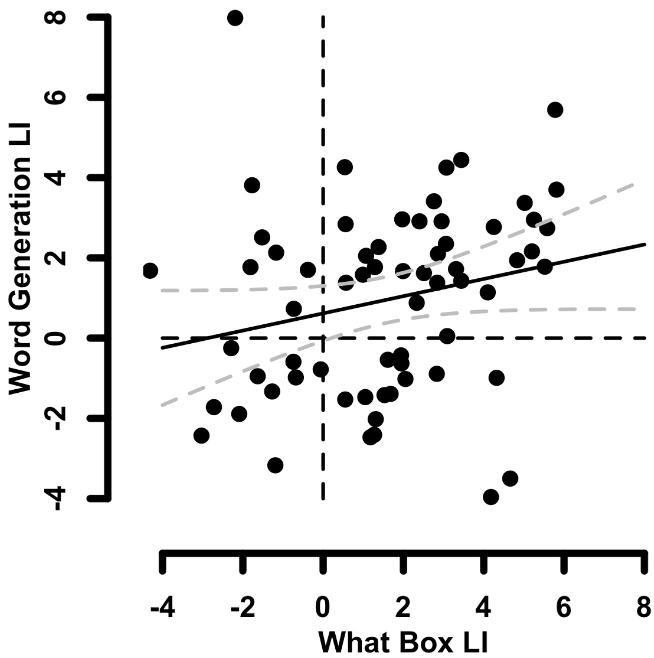

Figure 6. Scatter plot of the laterality indices (LIs) for the What Box and Word Generation tasks (n = 65). The linear regression line is fitted (solid line) with 95% confidence intervals (dashed grey lines).

Discussion

Here we report the methods and statistical characteristics of a child-friendly task for the assessment of language lateralisation using fTCD. The task presentation involves a face 'looking' for something, finding a box, the box opening, and an object appearing. Observers are prompted with "What's this?" and the label of the object, cueing overt and/or covert language production. This was successfully employed with young children aged between 1 and 5 years. Laterality indices (LIs) showed a broad distribution, with the group average indicative of left-lateralisation. In addition, a group of older adults completed the What Box task as well as the gold standard fTCD assessment for language lateralisation, Word Generation (Knecht, Deppe, Ebner, et al., 1998; Knecht et al., 1996). The LIs for both tasks were correlated, indicative of validity for the What Box task as invoking language processing.

The work adds to the methods available for assessing lateralisation using fTCD in children, including Picture Naming (Haag et al., 2010; Lohmann et al., 2005), Story Listening (Stroobant et al., 2011), and Animation Description (Bishop et al., 2009). Relative to the existing techniques, the internal reliability for the What Box – r = 0.64 [0.37 0.81] – was lower than Animation Description (r = .89 to .90 in 4-year-olds; Bishop, Holt, Whitehouse, & Groen, 2014; Bishop et al., 2009) and lower but comparable to Picture Naming depending upon the study (r = .88, Lohmann et al., 2005; Intra-class correlation = .66, Stroobant et al., 2011). It should be noted that the average number of accepted epochs was lower for What Box and the internal reliability was higher when more suitable epochs were available (n = 12, r = 0.69 [0.36, 0.87]; n = 14, r = 0.76 [0.36, 0.92]; see Supplementary Table 2). The fact that the What Box sample included younger children than other studies (previously down to 4 years of age), does not entirely account for this discrepancy as the adult sample also demonstrated lower reliability than the other task also conducted with adults. Therefore maximising the number of trials completed by children is recommended for reliability.

Despite the What Box producing left-lateralisation at the group level for children and adults, the index was relatively weak and only moderately correlated with Word Generation is adults. This is likely due to the low volume of production required is the task. Recently Payne and colleagues (2015) demonstrated that reduced rates of production are associated with weaker lateralisation. This pattern of behaviour likely accounts for the weaker lateralisation observed for the What Box task. Increasing the number of objects presented for labelling per trial may increase the lateralisation index as well as increase the correspondence between What Box and Word Generation. This is desirable considering the strength of the Word Generation task with respect to reliability (Knecht, Deppe, Ringelstein, et al., 1998; Stroobant & Vingerhoets, 2001) and validity (Knake et al., 2003; Knecht, Deppe, Ebner, et al., 1998; Somers et al., 2011).

As part of the data summary, we employed the latest version of an open source toolbox ("dopOSSCI", Badcock, Holt, et al., 2012), including artificial data clipping, activation correction, and activation separation epoch screening. We noted that due to the data-recording software settings, a minority of our data files did not record above 133 cm/sec. Using the artificial clipping of all other data files, we determined that this did not affect the LI calculations. Data recordings with less than 1% of values beyond -3 to 4 standard deviations were interpolated using a linear estimate between surrounding values (i.e., drawing a straight line between adjacent points). This resulted in the retention of data normally rejected as part of standard fTCD data screening techniques. With respect to activation separation epoch screening, epochs with a left-minus-right separation greater than 8%, affecting more than 1% of the data within an epoch, were removed from individuals' LI calculations. For the adult data, we used cut-offs sensitive to each individual's distribution of activation separations. This is a little-explored form of data screening that we found to maximise reliability calculations.

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We tested three baseline periods to establish the best processing methods for the What Box task: 1. -14 to -9 secs (time relative to stimulus), the presentation of a background image; 2. -9 to -4 secs, presentation of the animated face moving down the computer monitor; and 3. -4 to 1 secs, presentation of the animated face moving up the computer monitor. Relative to the end 'Shh' instruction of the previous trial, these periods were 0, 5, and 10 secs respectively. The task was stopped when the participant lost interest or became too fussy to continue. This resulted in between 1 and 32 acceptable epochs across the entire sample. Examination of the reliability for each baseline period as a function of the number of acceptable epochs indicated that the latest period was most consistent (-4 to 1, 10 secs after following the end of the previous trial). With reference to Figure 3, this is not surprising; the left-minus-right difference has normalised (i.e., no difference) by 10 seconds after the end of the previous trial. This is in line with neurovascular coupling estimates (Rosengarten et al., 2002). Future work may benefit from increasing the duration of the face-animation stages of the paradigm.

Future applications

Although What Box was designed for research with typically developing infants and toddlers, we also demonstrated its successful assessment of language lateralisation in older adults. The task is simple and may be conducted without verbal instructions. This provides a rare paradigm that can be applied across a broad age-range to map the development of lateralisation. Given the flexibility of the task, it will be useful in populations with atypical development such as dyslexia, specific language impairment, and Autism; where research has previously used the Word Generation in adults (dyslexia, Illingworth & Bishop, 2009; specific language impairment and autism, Whitehouse & Bishop, 2008). In addition, the simplicity of What Box makes it useful for working with populations where memory for and adherence to the rules associated with Word Generation limit its application; including, intellectual impairment (e.g., Down syndrome, Bowler, Cufflin, & Kiernan, 1985), cognitive decline such as aging (Keage et al., 2015), dementia (Matteis et al., 1998), and brain damage (Bragoni et al., 2000). TCD per se has been applied successfully in a wide range of populations (for systematic reviews see Bakker et al., 2014 in children, Keage et al., 2012 in aging and dementia), therefore the combination of fTCD and What Box provides a useful tool.

Conclusion

We report on a new method for the assessment of language lateralisation in young children that can also be used with adults. The method, the 'What Box' task, was successfully employed in children aged between 1 and 5 years using functional Transcranial Doppler Ultrasounds (fTCD) and corresponded well with Word Generation data collected with older adults. In addition to the methods, we present data collection and processing techniques for the efficient implementation and processing of the tasks for this population. The What Box task provides a suitable method for the assessment of language lateralisation in young children.

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References

Aaslid, R., Markwalder, T. M., & Nornes, H. (1982). Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. *Journal of Neurosurgery*, *57*(6), 769–774. http://doi.org/10.3171/jns.1982.57.6.0769

Badcock, N. A., Holt, G., Holden, A., & Bishop, D. V. M. (2012). dopOSCCI: a functional Transcranial Doppler Ultrasonography summary suite for the assessment of cerebral lateralization of cognitive function. *Journal of Neuroscience Methods*, *204*(2), 383–388. http://doi.org/10.1016/j.jneumeth.2011.11.018

Badcock, N. A., Nye, A., & Bishop, D. V. M. (2012). Using functional transcranial Doppler ultrasonography to assess language lateralisation: Influence of task and difficulty level. *Laterality*, *17*(6), 694–710. http://doi.org/10.1080/1357650X.2011.615128

Bakker, M. J., Hofmann, J., Churches, O. F., Badcock, N. A., Kohler, M., & Keage, H. A. (2014). Cerebrovascular function and cognition in childhood: a systematic review of transcranial doppler studies. *BMC Neurology*, *14*(43). http://doi.org/10.1186/1471-2377-14-43

Bishop, D. V. M., Holt, G., Whitehouse, A. J. O., & Groen, M. (2014). No population bias to left-hemisphere language in 4-year-olds with language impairment. *PeerJ*, *2*, e507. http://doi.org/10.7717/peerj.507

Bishop, D. V. M., Watt, H., & Papadatou-Pastou, M. (2009). An efficient and reliable method for measuring cerebral lateralization during speech with functional transcranial Doppler ultrasound. *Neuropsychologia*, *47*(2), 587–590. http://doi.org/10.1016/j.neuropsychologia.2008.09.013

Bookheimer, S. Y., Zeffiro, T. A., Blaxton, T. A., Gaillard, W. D., Malow, B., & Theodore, W. H. (1998). Regional cerebral blood flow during auditory responsive naming: evidence for cross-modality neural activation. *Neuroreport*, *9*(10), 2409–2413.

Bowler, D. M., Cufflin, J., & Kiernan, C. (1985). Dichotic listening of verbal and non verbal material by Down's syndrome children and children of normal intelligence. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *21*(4), 637–644.

Bragoni, M., Caltagirone, C., Troisi, E., Matteis, M., Vernieri, F., & Silvestrini, M. (2000). Correlation of cerebral hemodynamic changes during mental activity and recovery after stroke. *Neurology*, *55*(1), 35–40.

Dehaene-Lambertz, G. (2000). Cerebral specialization for speech and non-speech stimuli in infants. *Journal of Cognitive Neuroscience*, *12*(3), 449–460.

Deppe, M., Knecht, S., Henningsen, H., & Ringelstein, E. B. (1997). AVERAGE: a Windows® program for automated analysis of event related cerebral blood flow. *Journal of Neuroscience Methods*, *75*(2), 147–154. http://doi.org/16/S0165-0270(97)00067-8

Deppe, M., Knecht, S., Lohmann, H., & Ringelstein, E. B. (2004). A method for the automated assessment of temporal characteristics of functional hemispheric lateralization by transcranial Doppler sonography. *Journal of Neuroimaging: Official Journal of the American Society of Neuroimaging*, *14*(3), 226–230. http://doi.org/10.1177/1051228404264936

Deppe, M., Ringelstein, E. B., & Knecht, S. (2004). The investigation of functional brain lateralization by transcranial Doppler sonography. *NeuroImage*, *21*(3), 1124–1146. http://doi.org/10.1016/j.neuroimage.2003.10.016

Groen, M. A., Whitehouse, A. J. O., Badcock, N. A., & Bishop, D. V. M. (2011). Where were those rabbits? A new paradigm to determine cerebral lateralisation of visuospatial memory function in children. *Neuropsychologia*, *49*(12), 3265–3271. http://doi.org/16/j.neuropsychologia.2011.07.031

Gutierrez-Sigut, E., Payne, H., & MacSweeney, M. (2015). Investigating language lateralization during phonological and semantic fluency tasks using functional transcranial Doppler sonography. *Laterality: Asymmetries of Body, Brain and Cognition*, *20*(1), 49–68. http://doi.org/10.1080/1357650X.2014.914950

Haag, A., Moeller, N., Knake, S., Hermsen, A., Oertel, W. H., Rosenow, F., & Hamer, H. M. (2010). Language lateralization in children using functional transcranial Doppler sonography. *Developmental Medicine and Child*

Neurology, *52*(4), 331–336. http://doi.org/10.1111/j.1469-8749.2009.03362.x

Illingworth, S., & Bishop, D. V. M. (2009). Atypical cerebral lateralisation in adults with compensated developmental dyslexia demonstrated using functional transcranial Doppler ultrasound. *Brain and Language*, *111*(1), 61–65. http://doi.org/10.1016/j.bandl.2009.05.002

Keage, H. A. D., Churches, O. F., Kohler, M., Pomeroy, D., Luppino, R., Bartolo, M. L., & Elliott, S. (2012). Cerebrovascular Function in Aging and Dementia: A Systematic Review of Transcranial Doppler Studies. *Dementia and Geriatric Cognitive Disorders EXTRA*, *2*(1), 258–270. http://doi.org/10.1159/000339234

Keage, H. A. D., Kurylowicz, L., Lavrencic, L. M., Churches, O. F., Flitton, A., Hofmann, J., … Badcock, N. A. (2015). Cerebrovascular Function Associated With Fluid, Not Crystallized, Abilities in Older Adults: A Transcranial Doppler Study. *Psychology and Aging*. http://doi.org/10.1037/pag0000026

Knake, S., Haag, A., Hamer, H. M., Dittmer, C., Bien, S., Oertel, W. H., & Rosenow, F. (2003). Language lateralization in patients with temporal lobe epilepsy: a comparison of functional transcranial Doppler sonography and the Wada test. *NeuroImage*, *19*(3), 1228–1232.

Knecht, S., Deppe, M., Ebner, A., Henningsen, H., Huber, T., Jokeit, H., & Ringelstein, E. B. (1998). Noninvasive Determination of Language Lateralization by Functional Transcranial Doppler Sonography: A

Comparison With the Wada Test. *Stroke*, *29*(1), 82–86. http://doi.org/10.1161/01.STR.29.1.82

Knecht, S., Deppe, M., Ringelstein, E. B., Wirtz, M., Lohmann, H., Dräger, B., … Henningsen, H. (1998). Reproducibility of Functional Transcranial Doppler Sonography in Determining Hemispheric Language Lateralization. *Stroke*, *29*(6), 1155–1159.

Knecht, S., Henningsen, H., Deppe, M., Huber, T., Ebner, A., & Ringelstein, E. B. (1996). Successive activation of both cerebral hemispheres during cued word generation. *Neuroreport*, *7*(3), 820–824. http://doi.org/10.1097/00001756-199602290-00033

Kohler, M., Keage, H. A. D., Spooner, R., Flitton, A., Hofmann, J., Churches, O. F., … Badcock, N. A. (2015). Variability in lateralised blood flow response to language is associated with language development in children aged 1–5 years. *Brain and Language*, *145–146*, 34–41. http://doi.org/10.1016/j.bandl.2015.04.004

Lidzba, K., Schwilling, E., Grodd, W., Krägeloh-Mann, I., & Wilke, M. (2011). Language comprehension vs. language production: Age effects on fMRI activation. *Brain and Language*, *119*(1), 6–15. http://doi.org/10.1016/j.bandl.2011.02.003

Lohmann, H., Drager, B., Muller-Ehrenberg, S., Deppe, M., & Knecht, S. (2005). Language lateralization in young children assessed by functional transcranial Doppler sonography. *NeuroImage*, *24*(3), 780–790. http://doi.org/10.1016/j.neuroimage.2004.08.053

Malonek, D., Dirnagl, U., Lindauer, U., Yamada, K., Kanno, I., & Grinvald, A. (1997). Vascular imprints of neuronal activity: Relationships between the dynamics of cortical blood flow, oxygenation, and volume changes following sensory stimulation. *Proceedings of the National Academy of Sciences*, *94*(26), 14826 –14831.

Matteis, M., Silvestrini, M., Troisi, E., Bragoni, M., Vernieri, F., & Caltagirone, C. (1998). Cerebral hemodynamic patterns during stimuli tasks in multi-infarct and Alzheimer types of dementia. *Acta Neurologica Scandinavica*, *97*(6), 374–380.

Michel, G. F., Ovrut, M. R., & Harkins, D. A. (1985). Hand-use preference for reaching and object manipulation in 6- through 13-month-old infants. *Genetic, Social, and General Psychology Monographs*, *111*(4), 407–427.

Newell, D. W., & Aaslid, R. (1992). Transcranial Doppler: clinical and experimental uses. *Cerebrovascular and Brain Metabolism Reviews*, *4*(2), 122–143.

Nicholls, M. E. R., Thomas, N. A., Loetscher, T., & Grimshaw, G. M. (2013). The Flinders Handedness survey (FLANDERS): A brief measure of skilled hand preference. *Cortex*, *49*(10), 2914–2926. http://doi.org/10.1016/j.cortex.2013.02.002

Payne, H., Gutierrez-Sigut, E., Subik, J., Woll, B., & MacSweeney, M. (2015). Stimulus rate increases lateralisation in linguistic and non-linguistic tasks measured by functional transcranial Doppler sonography.

Neuropsychologia, *72*, 59–69. http://doi.org/10.1016/j.neuropsychologia.2015.04.019

Rosengarten, B., Osthaus, S., & Kaps, M. (2002). Overshoot and undershoot: control system analysis of haemodynamics in a functional transcranial Doppler test. *Cerebrovascular Diseases*, *14*(3-4), 148–152. http://doi.org/10.1159/000065672

Schumacker, R., & Muchinsky, P. (1996). Disattenuating correlation coefficients. *Rasch Measurement Transactions*, *10*(1), 479.

Somers, M., Neggers, S. F., Kahn, R. S., & Sommer, I. E. (2011). The measurement of language lateralization with functional transcranial Doppler and functional MRI: a critical evaluation. *Frontiers in Human Neuroscience*, *5*, 31. http://doi.org/10.3389/fnhum.2011.00031

Spearman, C. (1904). The proof and measurement of association between two things. *American Journal of Psychology*, *15*(1), 72–101.

Stroobant, N., Van Boxstael, J., & Vingerhoets, G. (2011). Language lateralization in children: A functional transcranial Doppler reliability study. *Journal of Neurolinguistics*, *24*(1), 14–24. http://doi.org/10.1016/j.jneuroling.2010.07.003

Stroobant, N., & Vingerhoets, G. (2001). Test-retest reliability of functional transcranial Doppler ultrasonography. *Ultrasound in Medicine & Biology*, *27*(4), 509–514.

Whitehouse, A. J. O., & Bishop, D. V. M. (2008). Cerebral dominance for language function in adults with specific language impairment or autism. *Brain*, *131*(12), 3193 –3200. http://doi.org/10.1093/brain/awn266

Wilke, M., Lidzba, K., Staudt, M., Buchenau, K., Grodd, W., & Krägeloh-Mann, I. (2005). Comprehensive language mapping in children, using functional magnetic resonance imaging: what's missing counts. *Neuroreport*, *16*(9), 915–919.

Supplementary Table 1

Stimulus list for infants and adults. Items are reported in columns by presentation order.

Infants		Adults		
baby	hat	clever	armour	sapphire
ball	horse	bread	scorpion	honey
banana	house	diamond	anchor	telephone
bath	light	scissors	key	camel
bed	milk	clover	bed	clock
bird	plane	owl	elephant	medal
biscuit	shoe	cabbage	mosquito	brick
book	sock	cake	ring	ambulance
bunny	teddy	skunk	pyramid	apple
bus	train	saxophone	ants	
cake	tv	bib	matches	
car	window	caravan	bomb	
cat		radio	limousine	
chair		atom	chair	
cow		scroll	mallet	
cup		cigar	armadillo	
dog		pencil	eggs	
door		dog	pineapple	
duck		plaster	chalk	
fish		shirt	jelly	
foot		cart	lute	

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Supplementary Table 2

Split-half reliability (Pearson product moment r values), 95% confidence intervals (CI), and laterality index (LI) descriptive statistics for three baseline periods (background = -14 to -9, face-down = -9 to -4, and face-up = -4 to 1) as a function of the minimum number of epochs included in the calculation. The descriptive statistics include: n = the number of participants included in the calculations, and LI values: mean and standard deviation (SD), and median and inter-quartile range (IQR).

Baseline Period	Min Epochs	n	LI mean (SD)	LI median (IQR)	r [95% CI]
Face-up	4	51	0.83 (2.24)	1.24 (3.54)	0.24 [-0.03, 0.49]
[-4 to 1]	6	40	0.92 (2.02)	1.23 (3.12)	0.46 [0.17, 0.67]
	8	33	0.71 (1.93)	1.24 (3.04)	0.59 [0.31, 0.78]
	10	29	0.87 (1.97)	1.3 (2.17)	0.64 [0.36, 0.82]
	12	20	0.97 (2.02)	1.4 (2.19)	0.69 [0.36, 0.87]
	14	13	0.8 (2.13)	1.3 (1.39)	0.76 [0.36, 0.92]
	16	13	0.8 (2.13)	1.3 (1.39)	0.76 [0.36, 0.92]
	18	8	1.53 (1.78)	1.78 (1.75)	0.75 [0.1, 0.95]
	20	5	2.15 (1.33)	2.46 (2.19)	0.64 [-0.56, 0.97]
Face-down	4	45	0.7 (2.16)	1.32 (3.58)	0.55 [0.31, 0.73]
[-9 to -4]	6	36	0.68 (1.91)	1.23 (3.2)	0.52 [0.23, 0.73]
	8	33	0.63 (1.92)	1.14 (3.24)	0.51 [0.2, 0.72]
	10	26	0.82 (1.81)	1.38 (2.89)	0.53 [0.18, 0.76]
	12	18	0.24 (1.82)	0.52 (3.29)	0.69 [0.33, 0.88]
	14	11	0.16 (2.02)	0.3 (3.34)	0.7 [0.17, 0.91]
	16	10	0.44 (1.89)	0.98 (2.84)	0.67 [0.07, 0.91]
	18	7	0.98 (1.53)	1.65 (2.2)	0.28 [-0.6, 0.85]
	20	4	0.84 (1.37)	1 (1.8)	0.34 [-0.92, 0.98]

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Baseline Period	Min Epochs	n	LI mean (SD)	LI median (IQR)	r [95% CI]
Background	4	43	0.03 (1.81)	0.1 (3.06)	-0.07 [-0.36, 0.24]
[-14 to -9]	6	35	0.11 (1.64)	0.28 (2.82)	-0.05 [-0.37, 0.29]
	8	32	0.05 (1.61)	0.19 (2.61)	-0.13 [-0.45, 0.23]
	10	23	-0.12 (1.44)	-0.32 (2.44)	-0.17 [-0.54, 0.26]
	12	18	0.07 (1.4)	0.38 (2.32)	-0.06 [-0.51, 0.42]
	14	11	0.25 (1.52)	0.98 (2.75)	0.29 [-0.38, 0.76]
	16	10	0.44 (1.46)	1.02 (2.74)	0.43 [-0.28, 0.83]
	18	8	0.45 (1.42)	1.02 (1.96)	0.29 [-0.52, 0.83]
	20	5	0.65 (1.47)	1.07 (2.41)	-0.1 [-0.9, 0.86]

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