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# Using functional transcranial Doppler ultrasonography to assess language lateralisation: Influence of task and difficulty level

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Language is lateralised to the left hemisphere in most people, but it is unclear whether the same degree and direction of lateralisation is found for all verbal tasks and whether laterality is affected by task difficulty. We used functional transcranial Doppler ultrasonography (fTCD) to assess the lateralisation of language processing in 27 young adults using three tasks: word generation (WG), auditory naming (AN), and picture story (PS). WG and AN are active tasks requiring behavioural responses whereas PS is a passive task that involves listening to an auditory story accompanied by pictures. We also examined the effect of task difficulty by a post hoc behavioural categorisation of trials in the WG task and a word frequency manipulation in the AN task. fTCD was used to measure task-dependent blood flow velocity changes in the left and right middle cerebral arteries. All of these tasks were significantly left lateralised: WG, 77% of individuals left, 5% right; AN, 72% left: 4% right; PS, 56% left: 0% right. There were significant positive relationships between WG and AN (r = 0.56) as well as AN and PS (r = .76) but not WG and PS (r = -0.22). The task difficulty manipulation affected accuracy in both WG and AN tasks, as well as reaction time in the AN task, but did not significantly influence laterality indices in either task. It is concluded that verbal tasks are not interchangeable when assessing cerebral lateralisation, but that differences between tasks are not a consequence of task difficulty.

Keywords: Lateralisation; Language; fTCD; Task difficulty.

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Functional transcranial Doppler ultrasonography (fTCD) is a quick and inexpensive, non-invasive method which can be used to assess cerebral lateralisation; in tasks such as language processing (Knecht, Deppe, Ebner, et al., 1998; Knecht et al., 1996). The technique compares blood flow velocity in the left and right middle cerebral arteries. These vessels are responsible for approximately 70% of the blood supply to each cerebral hemisphere (Deppe, Ringelstein, & Knecht, 2004; Ringelstein, Kahlscheuer, Niggemeyer, & Otis, 1990). FTCD is reliant on neurometabolic coupling: Task-dependent neural firing leads to a replenishment of metabolic resources, which can be estimated using the fTCD signal (Aaslid, Markwalder, & Nornes, 1982; Deppe, Knecht, Lohmann, & Ringelstein, 2004). A significant amount of research has been conducted examining language lateralisation using fTCD. In this paper we consider how the choice of task affects results.

Word generation (WG) is the gold standard task for assessing language lateralisation. The basic procedure involves a series of trials, each having a visual letter presentation, silent generation of words beginning with this letter, a verbal report of the generated words to establish task cooperation, and a period of rest to restore baseline states of activity (Knecht et al., 1996). With this task, left-hemisphere lateralisation for language is highly reproducible within individuals (Knecht, Deppe, Ringelstein, et al., 1998), and agrees well with findings from the Wada test (Knecht, Deppe, Ebner, et al., 1998) and magnetic resonance imaging (MRI) (Knecht, Deppe, & Ringelstein, 1999; Somers, Neggers, Kahn, & Sommer, 2011).

WG is a production task but reception of language is also important. Tasks assessing different components of language do not necessarily agree with respect to lateralisation. Recent fTCD studies have revealed varying lateralisation dependent on task, including WG, sentence construction, reading, semantic decision making, picture and video description, and listening to stories (Bishop, Watt, & Papadatou-Pastou, 2009; Haag et al., 2010; Stroobant, Van Boxstael, & Vingerhoets, 2010; Stroobant, Buijs, & Vingerhoets, 2009). Stroobant et al. (2009) used a story-listening task that involved listening to a 30-second story as the stimulus event, followed by answering some questions about the story. Compared with an expressive picture-description story-telling task (90% of individuals left-lateralised), the receptive task revealed less left dominance (60 to 75%, test-retest). Also using fTCD, Buchinger et al. (2000) compared lateralisation of productive versus receptive language tasks and found reduced lateralisation for the receptive task, consistent with evidence from alternate methods for the bilateral organisation of receptive language skills (e.g., Boatman et al., 1998, 1999; Desmond et al., 1995; Gallagher et al., 2008; Hertz-Pannier et al., 2002). While there is debate over the physical alignment of these two language processes (Gage et al., 2011; Moser, Papanicolaou, Swank, & Breier, 2011), lateralisation concordance with the Wada test is less reliable for receptive tasks and its associated brain regions (Kim & Chung, 2008; Lee, Legge, & Ortiz, 2003; Lesser, 2003; McDonald et al., 2009). The evidence suggests that productive or expressive tasks are more strongly lateralised than passive or receptive tasks; however, individual lateralisation varies between different expressive tasks also (Bishop et al., 2009) and expressive tasks are not always significantly lateralised at the group level (Haag et al., 2010). It is unclear how far this variation relates to individual strategies or task demands.

One factor of possible importance is task difficulty. It is not straightforward to make predictions about the impact of difficulty on lateralisation. It could be argued that increased difficulty will lead to increased lateralisation due to an increase in resources required by the specialised system. On the other hand it could be that as a task becomes more difficult there is recruitment of the non-specialised hemisphere, reducing lateralisation. Finally it is possible that the lateralisation of specific cognitive operations is fixed and that the specialised system is engaged to the same degree regardless of task demands. Dräger and Knecht (2002) examined the impact of difficulty on lateralisation using a WG task requiring participants to generate words from starting word strings; e.g., given "ST", street, stamp, stop. Difficulty was varied by manipulating the frequency of words commencing with particular strings. Although many more words were generated for easy word strings, fTCD lateralisation did not vary between conditions. However, the WG task involves two aspects: generation of words, and rehearsing them prior to recall. High-frequency strings would involve easy word finding, but a heavy load for rehearsal. Conversely, low-frequency strings would involve difficult word finding, but easy rehearsal. These effects could cancel each other out. Furthermore there may be individual differences in the strategy adopted, and the extent to which a participant focuses on rehearsal or generation. Bookheimer et al. (1998) used an auditory naming (AN) procedure that might guard against some of these differences. In the AN procedure participants are given a brief definition of a word and asked to name the word. The receptive, search, and productive demands of the tasks remain similar trial to trial. However, the search component can be manipulated by modifying the frequency of the described word.

An alternative task, requiring minimal instruction, is the picture story (PS) task, which was developed by Wilke et al. (2005) to assess language lateralisation in children. This involves the auditory presentation of stories, separated into short parts. The final word in each part is obscured by a tone (beep) and followed by a picture representing the obscured word. This encourages implicit word generation, although no verbal output is required. FMRI has identified the PS task to be left lateralised, including temporal

frontal activations (Wilke et al., 2005). The frontal activation, which is not seen when a non-beeped version of the task is used, can be interpreted as spontaneous and implicit word generation. Therefore the PS task provides a simple paradigm for the assessment of language lateralisation with minimal task requirements.

Because the AN and PS task have fewer task demands than WG, it is of interest to know whether they give equivalent results. Alternatively, if we find task differences we then need to ask if this reflects either poor reliability of the measure, task difficulty, or meaningful differences in laterality relative to task content. To address these questions we used three tasks to assess language lateralisation: WG, AN, and PS. Each task has different components. WG involves visual recognition of the letter stimulus, word finding, covert production, short-term memory and potentially covert rehearsal, and the component of interest is word finding, which is mixed with the productive and short-term memory components. AN involves verbal reception and comprehension, word finding, and overt production, and the component of interest is the word finding. Due to the compact nature of the AN procedure, all of these components may contribute to the resulting lateralisation. PS involves verbal reception and comprehension, visual recognition, and implicit production, and the component of interest is production.

We also assessed handedness of the participants as a variable that is weakly associated with language lateralisation. Knecht and colleagues (2000) found that the incidence of right-lateralisation for language was 25% in strongly left-handed individuals, decreasing linearly to 5% in strongly right-handed individuals. We included this measure to explore the relationship between handedness and lateralisation in the different language tasks.

### METHOD

#### Participants

A total of 28 participants was recruited from the university population. We failed to find a suitable temporal window to record a Doppler signal in one individual. The mean age of the final 27 participants was 26.56 (SD = 10.7, min: 20, max: 66); there were 9 males, and 4 reported writing with their left hand, 23 with their right hand.

#### Materials and procedure

A Doppler ultrasonography device (DWL Multidop T2: manufacturer, DWL Elektronische Systeme, Singen, Germany) was used to examine the blood-flow velocity through the left and right MCAs. Participants were fitted

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with a flexible head-set that held in place a 2-MHz transducer probe over each temporal skull window, and were seated at a viewing distance of approximately 120 cm from the screen. Experimental tasks were presented using a personal computer with a single, centrally aligned speaker and 21inch Digital VRC21-W3 monitor. The procedures were programmed using Matlab R2009a (Mathworks, Natick, MA, USA), which sent pulses to the Multidop system to denote trial onsets. The pulses in all tasks were sent using Cogent 2000 developed by the Cogent 2000 team at the FIL and the ICN and Cogent Graphics developed by John Romaya at the LON at the Wellcome Department of Imaging Neuroscience.

*Handedness.* Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971). Scores range from -100 to 100, left to right.

fTCD tasks.. The running order of the three fTCD tasks was counterbalanced and the entire procedure lasted approximately 1 hour and 20 minutes. Figure 1 gives a schematic summary of the three tasks.

*Word generation.* The word generation (WG) paradigm was based on Knecht et al. (Knecht, Deppe, & Ebner, et al. 1998; Knecht et al. 1996). There were 23 trials, one for each letter of the alphabet excluding Q, X, and Z. Each trial included a 5-second written "Clear Mind" instruction, 12.5 seconds of letter presentation with silent word generation, 5 seconds



**Word Generation** 

Figure 1. Schematic diagram of the Word Generation (upper panel), Auditory Naming (middle panel) and Picture Story (lower panel) trial sequence. Bold font represents in-task presentation of instructions; italicised represents events or responses.

where the participant was asked to say aloud the generated words, followed by 25 seconds of relaxation. A 500-ms event marker was sent to the Multi-Dop system at the onset of the letter presentation. All instructions were presented centrally in white Arial font on a black background.

Auditory naming. The auditory naming (AN) task was based on procedures used by Bookheimer et al. (1998). On each trial the participant heard a short definition and was asked to say the defined word as quickly as possible. High- and low-frequency words were selected from the whole English Corpus (http://ucrel.lancs.ac.uk/bncfreq/lists/5\_1\_all\_rank\_noun.txt) and definitions were devised using the Oxford English Dictionary. The average frequency of the high-frequency words was 767.5 (SD = 287.75) words per million and all low-frequency words occurred at 10 words per million. Definition length ranged from 2 to 6 words with an average length of 4.15 (SD = 1.19); there was no difference in length between the high- and lowfrequency words, t(19) < 0.1, p = 1. The average definition duration was 2.0 seconds (SD = 0.43) and there was no difference in duration between the high- and low-frequency definitions, t(19) = 1.4, p = 0.15.

Each trial included a 10-second visual "Clear Mind" instruction, an average 2-second auditory definition, a 5-second (maximum) interval for a verbal response, 3-second visual feedback of the correct word, and a 10-second "Relax" instruction. Immediately following the definition participants were asked to make a speeded, single-word, verbal response. The experimenter then recorded the reaction time with a keyboard key-press. Visual feedback was presented immediately after the key-press or after 5 seconds in the absence of a response. Feedback was provided to stop participants from continuing to think about the auditory description. A single trial took a maximum of 30 seconds. A 500-ms event marker was sent to the Multi-Dop system at the onset of the definition. All instructions were presented centrally in white Arial font on a black background.

*Picture story.* The picture story (PS) paradigm was based on that used by Wilke et al. (2005). The audio tracks of four stories were provided by the Imaging Research Centre at Cincinnati Children's Hospital Medical Centre (Vannest et al., 2009). These tracks were edited to provide 20 tracks, 5 for each story. The final word in each track was replaced by a 200-Hz sine wave using Audacity 1.2.6 (http://audacity.sourceforge.net). The mean time of each track was 5.6 seconds (SD = 0.79). These samples were presented with accompanying high-definition photographs representing the replaced words, set on black backgrounds. The stories were

presented in a random order across 20 trials, each lasting approximately 27 seconds.

Each trial included an auditory story (mean 5.6 seconds), a 2-second picture presentation, an 8-second rest interval, a 500-ms visual fixation, and an 11.5-second blank interval. The computer presented a black background throughout the presentation, with the exception of the picture and fixation presentations. The fixation consisted of 10 white concentric circles. In turn, each outer circle disappeared to maintain attention across the blank interval. A 500-ms event marker was sent to the Multi-Dop system at the onset of the story presentations. To assess attention to the task, 20 four-option multiple-choice questions, 5 for each story, were completed following this task. Participants were told that it was a passive task and they would hear a story accompanied by pictures.

The data were analysed using a custom Matlab program based Analvsis. on Average (Deppe, Knecht, Henningsen, & Ringelstein, 1997). This down-sampled the data from 100 to 25 Hz, adjusted mean left and right channel values to 100 on an epoch-by-epoch basis, performed heart cycle integration, and artefact rejection. Epochs including normalised values outside 60 to 140 were excluded as measurement artefacts. For each task, baseline-corrected, left minus right difference values were used to calculate laterality indices (LIs). Individual LIs were estimated by calculating the average left-right difference across a 2-second window centred on the maximum peak difference within a task-specific period of interest (POI) for all suitable epochs. Positive values indicate left lateralisation and negative values, right. Laterality categorisation (left, right, or bilateral) was tested using one-sample t-tests to determine whether individual LI values were significantly different from zero. Task-specific baseline and POI values (in seconds) were used relative the initial stimulus event markers; WG task: baseline = -15 to -5, POI = 3 to 13; AN task: baseline = -10 to 0, POI = 3 to 13; PS task: baseline = -8 to 0, POI = 5 to 17. The internal reliability of each task was estimated using Cronbach's  $\alpha$  (Cronbach, 1951), which should be interpreted as a correlation coefficient ranging from 0 to 1, with higher values indicating higher reliability. Reliability estimates were based on LIs calculated independently for each epoch. Two further physiological indices are reported: mean activation and LI latency. The mean activation was calculated as the average left and right blood flow velocity relative to baseline levels at the peak left minus right difference and LI latency reflects the time in seconds of the peak left minus right difference, relative to the onset of the stimulus.

Task difficulty analysis. Additional summaries were conducted for the WG and AN tasks to assess the effect of task difficulty on lateralisation indices. In the WG task, letters were grouped into three difficulty levels based on the average number of reported words for the whole group of participants. In the AN task, trials corresponding to the high- and low-frequency word definitions were taken to correspond to low and high difficulty levels respectively.

#### RESULTS

The number of suitable data sets varied between tasks due to insonation difficulties. There were a total of 22 individuals' data for WG, 25 for AN, and 27 for PS. Within task analyses of variance indicated no significant effects of task order (all F < 1). For the WG task participants reported an average of 4.18 (SD = 0.38, min: 1, max: 7) words per letter. In the AN task the overall accuracy was 64% correct. For the PS task post-test accuracy was 90% correct (median = 95, SD = 10, min 60, max 100). These behavioural data confirmed that participants attended to all tasks.

Baseline corrected Doppler velocities for the left and right hemisphere activation, as well as the left minus right difference are presented for each task in Figure 2. The descriptive statistics for each task are presented in Table 1. At the group level, all tasks produced significantly left-lateralised blood flow. It is also possible, using the one-sample *t*-tests for each individual, to categorise their lateralisation as left, right, or bilateral. Both the overall task LIs and the individually significant left LIs, indicated the WG (77% of participants) and AN (72%) tasks to be more strongly lateralised than the PS task (56%). None of the LIs was significantly related to handedness (see Table 1).

The LIs for each task were not significantly different (paired-sample *t*-tests), although there was a trend for higher LIs in WG and AN compared with PS: WG:AN, t(20) = -0.25, p = 0.81, Cohen's d = -0.07; WG:PS, t(20) = 1.98, p = 0.06, Cohen's d = 0.61; AN:PS, t(24) = 2.04, p = 0.05, Cohen's d = 0.39. The relationships between task LIs is depicted in Figure 3. WG was not significantly related to either AN or PS and there was a positive relationship between AN and PS; WG and AN r = .32 (ns), WG and PS, r = -.13 (ns), and AN and PS, r = .55 (p < .01). One multivariate outlier was removed from the WG correlations; however, this did not influence the relationships. Although there was only one correlation, between AN and PS, that reached statistical significance, it should be noted that these correlations need to be corrected for attenuation; i.e., the imperfect reliability of the measures (Spearman, 1904). The internal reliability estimated using Cronbach's alpha were 0.52 for WG, 0.77 for AN, and 0.68 for PS. When correlation for attenuation was made using these values, the correlation



Figure 2. Word Generation, Auditory Naming, and Picture Story left and right hemisphere activation (left half) and left-right difference activation (right half) at a function of epoch time in seconds. Mean Laterality Indices (LI) are displayed in the difference graphs with standard deviation in brackets. All values are accompanied by \* to indicate statistical difference from 0 at p < .05. For the difference activation error bars depict the standard error of the mean.

		Word generation	Auditory naming	Picture story
	n	22	25	27
Trials	Mode	23	40	20
	Min	20	34	17
	Total	23	40	20
Reliability (Cronbach's a)		0.52	0.77	0.68
LI	Mean	2.41*	2.49*	1.62*
	SEM	0.35	0.48	0.43
Left†	n (%)	17 (77)	18 (72)	15 (56)
Right <sup>†</sup>		1 (5)	1 (4)	0 (0)
Bilateral†		4 (18)	6 (24)	12 (44)
LI:Handedness	Spearman's Rho	.37	050	09

#### TABLE 1

Task statistics including *N* accepted trials, internal consistency, Laterality Indices (LI) and lateralisation counts (left, right, and bilateral), as well as the relationship between LIs and handedness.

\*p < .01, for one-sample *t*-tests against 0.

 $\dagger$ Categorisation of laterality status is based on one-sample *t*-tests for each individual testing whether L–R activation across epochs differs significantly from zero.

between WG and AN rises to .56 (p < .05), and that between AN and PS rises to .76 (p < .001). The negative association between WG and PS remains non-significant at -.22.

## Task difficulty

*Word generation.* For WG, letter groupings based on average group report were low: K U Y N O J V I, M = 3.77 (SD = 0.26); medium, A E C W F P R G: M = 4.25 (SD = 0.12); and high, L T H M S B D: M = 4.56 (SD = 0.14).

LIs, mean left right activations, and peak left minus right difference latencies are displayed by word production grouping in the top row of Figure 4. None of the differences was statistically significant: repeated measures ANOVAs; LI,  $F(2, 42) = 0.25 \ p = 0.78$ ,  $\eta_p^2 = 0.01$ ; mean activation,  $F(2, 42) = 1.53 \ p = 0.23$ ,  $\eta_p^2 = 0.07$ ; and latency,  $F(2, 42) = 0.79 \ p = 0.46$ ,  $\eta_p^2 = 0.04$ . Thus word production is not related to the physiological LI, mean activation, or peak latency of silent word generation in the WG task.

Auditory naming. In the AN task responses were more accurate and faster to the high-frequency words in comparison to the low-frequency words; accuracy as proportion correct: High, M = 0.69, SD = 0.09; Low, M = 0.60, SD = 0.10; and reaction time in seconds: High, M = 1.81, SD = 0.36; Low,



Figure 3. Individual laterality index scatter plots between task; Top: Word Generation (WG) versus Auditory Naming (AN), Middle: WG versus Picture Story (PS), and Lower: AN versus PS. The data points for left-handed individuals are filled in black. Disattenuated Pearson product moment correlations coefficients are presented for each relationship excluding the outlier (grey fill) for the WG comparisons (\*p <.05, \*\*p <.001).

M = 2.37, SD = 0.53. Both of these effects were statistically significant; accuracy, t(24) = 4.16, p < .001, Cohen's d = 0.99; reaction time, t(24) = 7.99, p < .001, Cohen's d = -1.26. Therefore the word frequency manipulation was successful, behavioural responses indicating that descriptions of high-frequency words were more easily and rapidly named in comparison to low-frequency words.

LIs, mean left right activations, and peak left minus right difference latencies are displayed by word frequency in the bottom row of Figure 4. None of the differences was statistically significant: paired sample *t*-tests; LI, t(24) = 0.29, p = 0.77, Cohen's d = 0.05; mean activation, t(24) = 0.77, p = 0.45, Cohen's d = 0.14; and latency, t(24) = 1.65, p = 0.11, Cohen's d = -0.4. This indicates that word frequency is not related to the physiological LI, mean activation, or peak latency of word finding in the AN task.

Picture story. Although no behavioural manipulation was conducted for the PS task, we were able to consider whether individual differences in posttest accuracy affected LI. Accuracy was unrelated to LI (Spearman r = 0.36), mean activation (Spearman r = 0.17), or LI latency (Spearman r = 0.11).

#### DISCUSSION

Participants completed three language tasks in an fTCD paradigm: word generation (WG), auditory naming (AN), and picture story (PS). WG required participants to silently generate words to a visually presented letter, AN required participants to verbally report a single word from an auditory definition, and PS required participants to passively listen to stories accompanied by pictures depicting acoustically masked words from the stories. All tasks were left lateralised, WG and AN more clearly with respect to the number of left-lateralised individuals, 77 and 72% respectively, than PS (56%). Furthermore, behavioural responses were unrelated to physiological responses, despite significant behavioural differences due to task difficulty.

WG is commonly used for assessing language lateralisation and has been validated in fTCD with respect to the Wada technique (Knecht, Deppe, Ebner, et al., 1998) and fMRI (Knecht et al., 1999). Each trial is relatively long and participants report many different approaches to the task: some rehearsing a small set of words, others chunking sentence-like combinations of words, and some reporting new words that were not silently generated. Therefore, while the component of interest is the word finding, the activity due to the additional components (visual recognition, covert productive, short-term memory rehearsal) is likely to vary between individuals and







706 BADCOCK, NYE, BISHOP potentially within individuals. Furthermore the long periods during which participants are required to "clear their minds" varies in reported ease between participants. This variability may be reflected in the mean left–right activation at peak difference (see Figure 4). There is large variability in this task, mean activity varying from much lower than baseline to much higher than baseline. Decreases may reflect concerted efforts to think of nothing during periods of baseline and normalisation, whereas others may find this simple. This is not the case with the AN and PS paradigms, mean activation predominantly (all but one individual) being positive. This may reflect greater consistency in task approach.

One of the clear advantages of the AN task is the duration of the procedure. Approximately double the number of AN trials were run relative to the WG task in the same time period. PS was also a much shorter task. Potentially, the larger number of trials will reduce noise in the data and could underpin the significant relationship between AN and PS. Previous research has identified lateralisation differences as well as varying relationships between language tasks using fTCD (Buchinger et al., 2000; Haag et al., 2010; Stroobant et al., 2009; Stroobant et al., 2010). These studies have examined word fluency (similar to WG), sentence construction, reading, semantic decision making, picture description, and story listening. All studies have found variability between tasks and varying relationships between them, consistent with our current results. In a story-listening task with children consisting of 30 seconds of listening followed by questions, Stroobant et al. (2010) found equivalent left lateralisation as with our own PS task. Therefore our findings are consistent with prior research, which has shown that expressive tasks are more strongly lateralised than receptive tasks. However, different expressive tasks are not interchangeable; it seems that direction and degree of lateralisation can vary from task to task within individuals, and that this is not totally explicable in terms of poor task reliability or variations in task difficulty. Previous work suggests that receptive language is more bilaterally distributed (Boatman et al., 1999, 1998; Buchinger et al., 2000; Hertz-Pannier et al., 2002); we suggest that the relatively low LI scores in the PS task may reflect weaker or inconsistent activation of implicit production in this task compared to the AN or WG tasks.

The major limitation of this research is restricted range for the laterality indices, and the low internal reliability of the tasks. The sample included few left-handed individuals and only two individuals demonstrated significant right lateralisation on any of the tasks, neither individual showing consistently right activity between tasks. Greater within sample variability may have shown a stronger relationship between tasks; however, it is unlikely to affect the findings of the difficulty manipulation. Relative to previously reported internal reliability of fTCD language tasks (e.g., around .9 in Bishop et al., 2009), the reliability of our tasks was low (.52 to .77). This will attenuate the observed correlation between tasks, although we were able to apply a standard attenuation correction to take this into account. Future investigations could adopt a targeted approach to subject recruitment, actively seeking left-handed individuals to increase the likelihood of atypical lateralisation (see Knecht et al., 2000).

In conclusion, language lateralisation derived from performing expressive and receptive procedures varies between tasks, expressive tasks demonstrating the highest degree of lateralisation. Differences were not explained by task difficulty but may be due the balance of expressive and receptive language demands. It may be best to use tasks that minimise the possibility of participants adopting idiosyncratic task-specific strategies.

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