Supplement to Zooming in on abnormal local and global processing biases after stroke: Frequency, lateralization, and associations with cognitive functions

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Appendix A. Description of neuropsychological tasks

Catherine Bergego Scale: The Catherine Bergego Scale is an observation scale for neglect in activities of daily living (Azouvi et al., 2003; Ten Brink et al., 2013). It assesses performance in personal, peripersonal, and extrapersonal space. For 10 items, neglect severity has to be scored, resulting in a total score of 0 (no neglect) to 30 (severe neglect).

Line bisection: The line bisection task assesses lateralized inattention. The task consists of three horizontal lines (22° long and 0.2° thick) that are presented upper right, lower left, and in the horizontal and vertical centre of a computer screen (Van der Stoep et al., 2013). The amount of horizontal shift between lines is 15% of the line length. The stimulus presentation is approximately 19° wide and 5.7° high. Patients have to click on the midpoint of each line using a computer mouse. The three lines are presented four times in a row, after which the absolute average deviation from the midpoint is calculated for all trials, ranging from 0° (no lateralized attention bias) to 11° (severe lateralized attention bias). The task was administered in near space (i.e., 30 cm) and far space (i.e., 120 cm).

Balloons Test: This task is designed to detect lateralized inattention (Edgeworth, Robertson, & McMillan, 1998). In subtest B, 180 balloons (circles with a vertical line in the lower part) and 20 circles are presented on an A3 paper. Participants have to mark all circles. The laterality score of subtest B (ranging from 0% to 50%, higher scores indicating better performance) was used as an outcome measure for lateralized attention bias.

Shape cancellation: A digitized shape cancellation task was used to assess lateralized inattention. The stimuli consisted of 54 small targets (0.6° × 0.6°), 52 large distractors, and 23 words and letters (widths ranging from 0.95° to 2.1° and heights ranging from 0.45° to 0.95°). The stimulus presentation was approximately 18.5° wide and 11° high. Patients were seated 120 cm in front of a monitor and used a computer mouse. They were instructed to click all targets and tell the examiner when they had completed the task. No time limit was given. We administered a version in which marks appeared at all clicked locations (i.e., feedback) and one where no marks appeared (i.e., no feedback). The horizontal normalized Centre of Cancellation (CoC-x) was computed, reflecting both the location and the number of cancelled targets. The CoC-x ranges from −1 to 1. The absolute CoC-x was used, resulting in a range of 0 (no lateralized attention bias) to 1 (severe lateralized attention bias). In addition, we assessed the organization of search by computing the intersections rate. We computed the number of lines that crossed paths between previously cancelled targets, divided by the total number of cancellations that were not immediate revisits (i.e., formulas are described in Dalmaijer et al., 2014, Eqs. 3-8). An organized search pattern includes as few intersections as possible, resulting in a low value for intersections rate. Outcome measures were computed using the CancellationTools software (Dalmaijer et al., 2014).

Trail Making Test: The Trail Making Test (TMT)-A and TMT-B subtests are used to examine visual search speed (Bouma, Mulder, Lindeboom, & Schmand, 2012). The TMT-A subtest consists of a set of 25 circles that contain numbers (1 to 25). Instructions are to connect the circles in ascending order as fast as possible. In the TMT-B subtest, the participant has to alternate between numbers and letters (1 – A – 2 – B, etc.). For both subtests, the total duration is recorded, with longer durations reflecting slower search. A corrected score for the TMT-B subtest is computed to reflect switching, in which the duration of the TMT-A is taken into account (a higher ratio score indicates more interference of the switching).

Rey Complex Figure Test: The Rey Complex Figure Test copy was designed to diagnose disorders in visuospatial perception and visuo-construction (Bouma et al., 2012; Rey, 1941). Participants are asked to copy the Rey Complex Figure. The accuracy of the drawing is scored based on clearly defined criteria. The total score ranges from 0 (none of the elements were accurately copied) to 36 (perfectly accurate copy).

Tower Test: The Tower Test (Delis, Kaplan, & Kramer, 2007) measures spatial planning, rule learning, inhibition of impulsive and perseverative responding, and the ability to establish and maintain an instructional set. Participants are presented with a board containing three vertical pegs, and five disks with varying diameters. At each of nine trials, an example tower has to be built, and the participant has to obey certain rules. The total score is based on a scoring system which depends on the number of steps per trial (range 0-30), with higher scores indicating better performance.

Brixton Test: The Brixton Spatial Anticipation Test ('Brixton Test') is a visuospatial sequencing task with rule changes (Burgess & Shallice, 1997). It measures rule switching and spatial prediction. Participants are presented with 56 pages, each containing an array of ten circles set in two rows of five, with each circle numbered from 1 to 10. One of the circles is filled with a blue colour. The participant is shown one page at the time. The position of the blue circle differs per page, and participants have to indicate where they think the blue circle will be located on the next page. The locations are governed by a series of simple rules that change without warning. The total number of errors was computed (range 0-55), with higher scores reflecting worse performance.

Digit Span: The Digit Span subtest from the Wechsler Adult Intelligence Scales (WAIS), versions WAIS-III-NL and WAIS-IV-NL consists of two parts: forward and backward (Wechsler, 2012). The test administrator reads out loud a series of digits. Participants either have to repeat the sequence in the same order (Digit Span forward), reflecting short-term verbal memory, or they have to repeat the sequence backwards (Digit Span backward), reflecting verbal working memory. Each part consists of eight items of each two series, that increase in length up to a maximum of 10 digits. The longest sequence that was correctly repeated was used as an outcome measure (range 2-10), with higher scores reflecting better performance.

Rey Auditory Verbal Learning Test: The Rey Auditory Verbal Learning Test (RAVLT) is used to measure verbal long-term memory (Bouma et al., 2012). Fifteen words are read out loud, after which the participant has to repeat as many words as possible.

This procedure is repeated 5 times (immediate recall score, the total number of correct words ranges from 0-75). After a delay of 15-30 minutes, participants are asked to recall as many words as possible (delayed recall score, ranging from 0-15). For the recognition phase, a list of 30 words (15 old, 15 new) is presented and participants have to indicate for each word whether it was in the original list (recognition score, ranging from 0-30). For all RAVLT outcomes, higher scores reflect better performance.

Appendix B. Supplementary Tables and Figures

Supplementary Table 1. The minimum stimulus duration for each individual participant in the local and global conditions of the **directed attention task**, for **healthy subjects** (*n* = 34). There were 6 blocks, and participants started with a stimulus duration of 1000 ms. If 3 or more errors were made, the stimulus duration in the consecutive block would increase, whereas it would decrease if less than 3 errors were made.

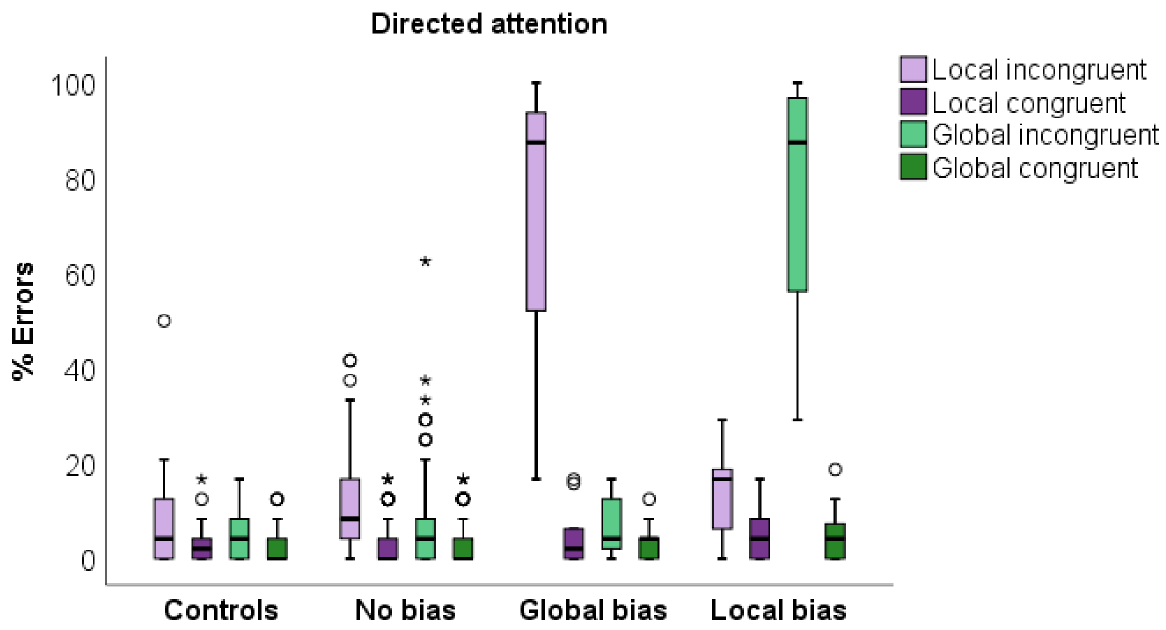
		Global				
		150 ms	250 ms	500 ms	750 ms	1000 ms
Local	150 ms	31	1			
	250 ms	1				
	500 ms					
	750 ms					
	1000 ms	1				

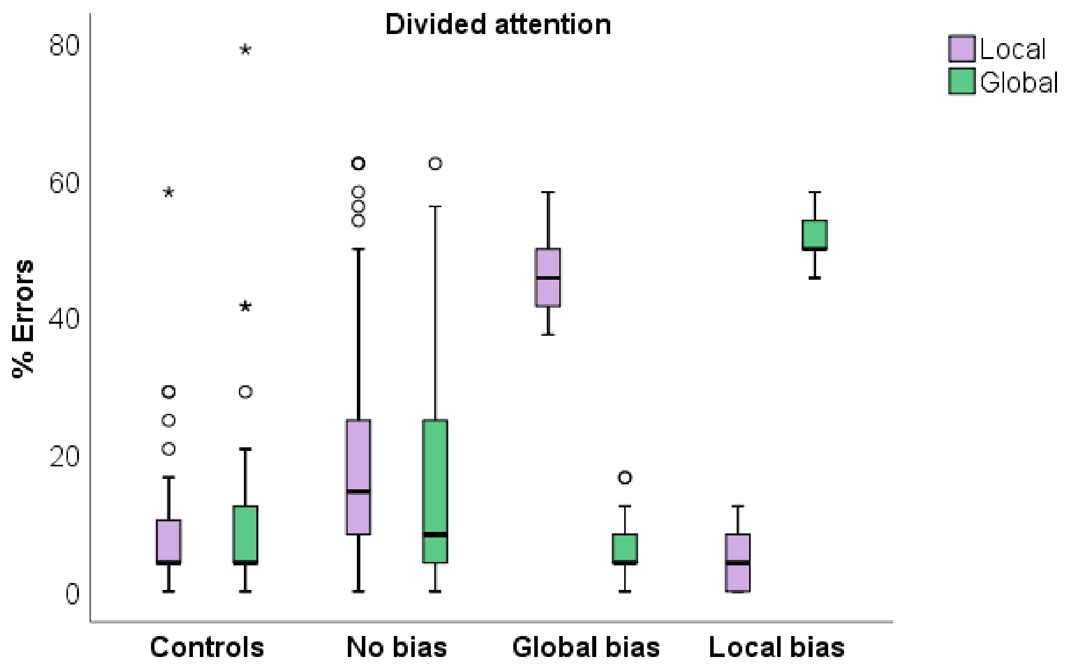
Supplementary Table 2. The minimum stimulus duration for each individual participant in the local and global conditions of the **directed attention task**, for **stroke patients** (*n* = 192). There were 6 blocks, and participants started with a stimulus duration of 1000 ms. If 3 or more errors were made, the stimulus duration in the consecutive block would increase, whereas it would decrease if less than 3 errors were made.

		Global				
		150 ms	250 ms	500 ms	750 ms	1000 ms
Local	150 ms	149	8	2	2	8
	250 ms	7	1		3	1
	500 ms					1
	750 ms	4				
	1000 ms	6				

Supplementary Table 3. The minimum stimulus duration for each individual participant in the **divided attention task**, for **healthy subjects** (*n* = 35) and **stroke patients** (*n* = 258). There were 6 blocks, and participants started with a stimulus duration of 1000 ms. If 3 or more errors were made, the stimulus duration in the consecutive block would increase, whereas it would decrease if less than 3 errors were made.

		Healthy	Stroke
Divided	150 ms	28	153
	250 ms	5	55
	500 ms	2	12
	750 ms		15
	1000 ms		23





Supplementary Figure 1. Upper graph: Boxplots showing the percentage of errors, split for the local and global conditions, and congruent and incongruent trials of the directed attention task, depicted for healthy controls (n = 34), stroke patients without a bias (n = 165), with a global bias (n = 12), and with a local bias (n = 15). Lower graph: Boxplots showing the percentage of errors, split for the local and global conditions, in the divided attention task, depicted for healthy controls (n = 35), stroke patients without a bias (n = 227), with a global bias (n = 17), and with a local bias (n = 14). Groups are defined based upon the mean ± 3 *SD* from performance of controls. The thick line in the middle is the median. The top and bottom box lines show the first and third quartiles. The whiskers show the maximum and minimum values, with the exceptions of outliers (circles) and extremes (asterisks).

Appendix C. Supplementary analyses

Local and global interference in left- versus right-sided brain damaged stroke patients: effects of presentation side

For the directed attention task, a repeated measures ANOVA was conducted with lesion side (left, right) as between subjects-factor and condition (local, global), congruency (congruent, incongruent), and presentation side (left, right) as within-subjects factors. The dependent variable was error rate. Age and sex were included as covariates. We evaluated the interaction effect of lesion side * condition * presentation side, and lesion side * condition * congruency * presentation side to assess whether bias and/or interference effects differed between patients with left or right sided brain lesions. There were no interaction effects of lesion side * condition * presentation side, $F(1) = 1.12$, $p = .292$, $\eta^2 = .01$, nor for lesion side * condition * congruency * presentation side, $F(1) = 1.33$, $p = .252$, $\eta^2 = .02$.

We additionally ran post-hoc tests for the left- and right-sided lesion groups separately to directly assess the effect of presentation side within each group. There was no interaction between condition * congruency * presentation side for patients with left-sided lesions, $F(1) = 0.35$, $p = .557$, $\eta^2 = .01$, nor for patients with right-sided lesions, $F(1) = 0.12$, $p = .732$, $\eta^2 = 0$,

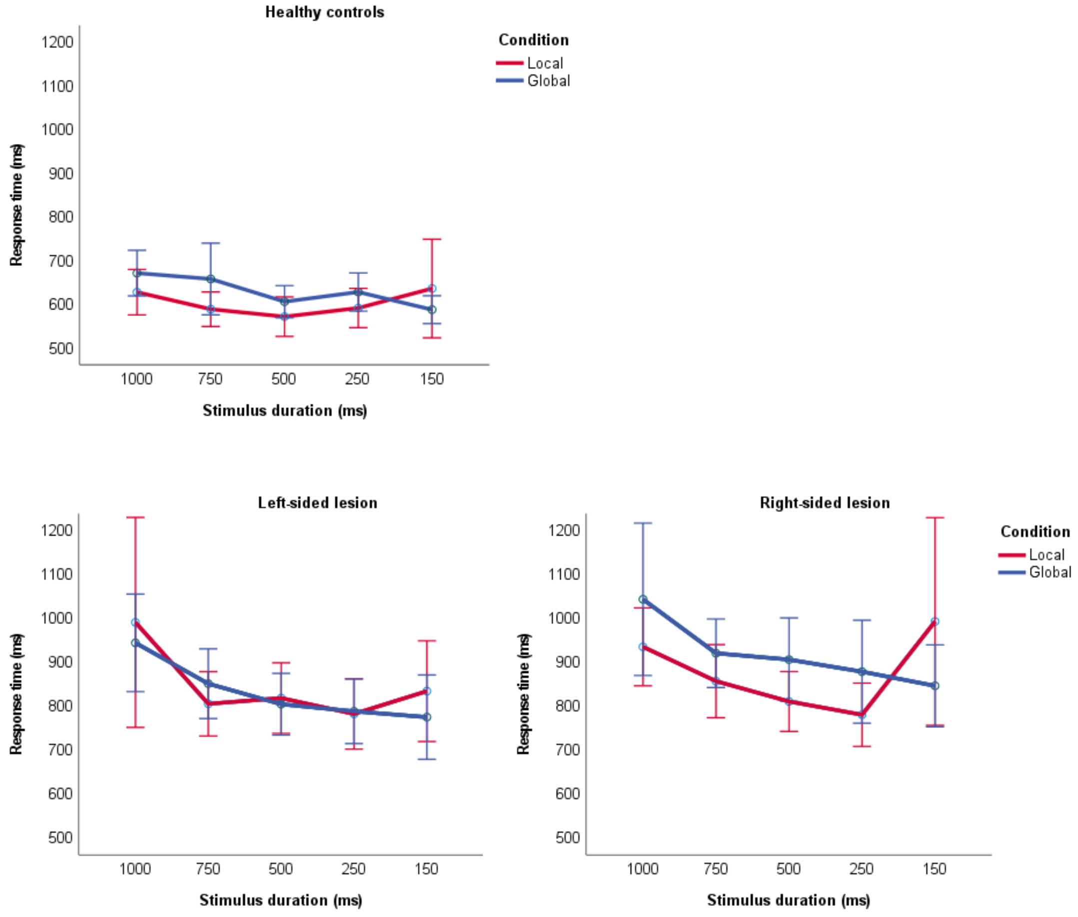
Local and global bias in left- versus right-sided brain damaged stroke patients: reaction time

The median reaction time (RT) per stimulus duration in the directed attention task is plotted in Supplementary Figure 2, split for healthy controls, patients with a left-sided brain lesion, and patients with a right-sided brain lesion. Patients who made ≥3 errors in two or more blocks were not included in this sample, since no data was available for the stimulus duration of 150 ms. Thus, the most severely affected patients were excluded.

For RT at the directed attention task, a repeated measures ANOVA was conducted with lesion side (left, right) as between subjects-factor and condition (local, global), congruency (congruent, incongruent) as within-subjects factors. Stimulus duration (i.e., 150, 250, 500, 750, 1000), age, and sex were included as covariates.

We evaluated the interaction effect of lesion side * condition * congruency, to assess whether interference effects differed between patients with left or right sided brain lesions. There was no interaction effect of lesion side * condition * congruency, $F(1) = 1.086$, $p = .301$, $\eta^2 = .02$.

We conducted a sensitivity analysis including only blocks in which the stimulus duration was 150 ms, since effects on RT might have been largest with shortest stimulus duration. There was no interaction effect of lesion side * condition * congruency, $F(1) = 2.41$, $p = .126$, $\eta^2 = 0.03$.



Supplementary Figure 2. Line graphs depicting the average of median reaction times (ms) split for the local and global conditions, and the different stimulus durations of the directed attention task, depicted for healthy controls (n = 31 out of 34), and stroke patients with left-sided (n = 37 out of 46) and right-sided brain lesions (n = 36 out of 48) who reached the final stimulus duration (i.e., 150 ms) in the staircase. Values are corrected for age and sex. Error bars indicate 95% confidence intervals.

Supplementary Table 4. Spearman correlation coefficients between *local and global interference scores* derived from the directed attention task, the *absolute bias score* derived from the divided attention task, and performance at tasks for lateralized attention. Higher interference scores indicated more interference from the irrelevant level (i.e., higher local interference scores indicate a stronger local bias; higher global interference scores indicate a stronger global bias). Higher absolute bias scores in the divided attention task indicate more difficulties with attending the local and global level simultaneously. For the line bisection task, positive scores indicate deviation towards the right (i.e., leftward bias). For the shape cancellation task, positive scores indicate more omissions on the left than the right (i.e., leftward bias).

		Directed attention			**Divided attention**
	***n*[1]**	**Global interference**	**Local interference**	***n*[1]**	**Absolute bias score**
Lateralized attention					
Line bisection near, deviation	188	*r* = -.04, *p* = .545	*r* = -.11, *p* = .118	246	*r* = -.04, *p* = .563
Line bisection far, deviation	188	*r* = .05, *p* = .486	*r* = .07, *p* = .336	246	*r* = .01, *p* = .917
Shape cancellation feedback, CoC-x	187	*r* = .06, *p* = .482	*r* = .13, *p* = .075	243	*r* = 0, *p* = .969
Shape cancellation no feedback, CoC-x	183	*r* = .15, *p* = .040*	*r* = .04, *p* = .612	237	*r* = .02, *p* = .805

Abbreviations. CoC-x, horizontal centre of cancellation.

[1]Group sizes differ between measures since not all patients performed all neuropsychological tasks.

* Significant with alpha = 0.05

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