

Supplementary Methods

Visuospatial Attention

To assess visuospatial attention, the Letter Cancellation Test,¹ the Line Bisection Test,² the Five-Point Test,³ and video-oculography during free visual exploration (FVE^{4,5}) were performed.

In the **Letter Cancellation Test**¹, patients were required to cancel 60 target letters “A”, distributed among distractor letters. The Center of Cancellation (CoC) was calculated using the freely available software provided by Rorden and Karnath (<https://www.mccauslandcenter.sc.edu/crnl/tools/cancel>). The CoC allows to quantify visuospatial attention deployment by taking into account the number of omissions as well as their spatial distribution.⁶

In the **Line Bisection Test**,² patients were asked to mark the middle of 12 horizontal lines of different length, pseudo-randomly distributed along the horizontal axis and printed on an A3 landscape-oriented paper. The mean relative rightward deviation (in percentage, %) was calculated.

In the **Five-Point Test**,³ patients were required to generate as many different designs as possible within 3 minutes. Designs should be generated by connecting at least two out of the five dots, each set of dots being presented in a separate rectangle, by means of straight lines. The CoC was calculated for the spatial distribution of all designs, as previously described.⁷

Video-oculography during **FVE** was performed in order to assess the spatial distribution of visual fixations along the horizontal axis.^{4,5,8-10} In short, 24 photographs of natural scenes or urban public places, and their mirrored versions (mirrored along the vertical axis), were presented on a screen, each for 7 sec. To enforce a common central starting point of visual exploration, each photograph was preceded by a black fixation-cross in the middle of the screen, presented for 3 sec. During the experiment, patients were instructed to freely explore the images. In the offline analysis, only fixations with a duration of 100 – 2,000 msec were included.^{11,12} The mean gaze position on the horizontal axis (in ° of visual angle) was calculated as outcome variable.^{5,10,13}

Alertness

Four variables commonly thought to reflect alertness were included in the present study: two subtest of a computerized, validated attention test battery (*Testbatterie für die Aufmerksamkeitsprüfung*, TAP; tonic and phasic Alertness¹⁴) and two outcome variables of the FVE paradigm (mean fixation duration,¹¹ and peak saccade velocity¹⁵).

For the TAP computerized assessment of tonic alertness, patients were presented with a central fixation point (presentation duration randomly varying between 3,000–5,000 msec), followed by a X (target) presented at the same position. At target appearance, patients were required to press a button as quickly as possible, and reaction time was recorded. In the phasic alertness assessment, a warning tone was presented at a randomly determined time interval of 650–1240 msec before the target. Patients performed 4 blocks of the task (2 for tonic and 2 for phasic alertness), with 20 trials each, in an ABBA design, starting with the condition without warning tone. For both **TAP phasic alertness** and **TAP tonic alertness**, the patients' individual median reaction time over all trials was calculated, as implemented in the computerized TAP analysis tool.¹⁴

To investigate alertness within the FVE paradigm, the patients' individual **mean fixation duration**^{13,16} was calculated over the whole course of visual exploration. Additionally, the mean **peak saccade velocity** in the FVE paradigm¹⁷ was calculated, based on the saccade report provided by the parsing algorithm of the eye tracking system.

Inhibition

Four tests reflecting inhibition were included, as described in previous studies: three neuropsychological measures (perseverative errors in the Five-Point Test,³ a Go-Nogo task,^{18,19} the Stroop interference task^{20,21}) and one video-oculography measure (false responses in the antisaccade task^{22,23}).

In the **Five Point Test**, the repeated drawing of the same design (perseverative errors) was used to quantify inhibition failure, as previously described.^{7,24} To this end, the percentage of perseverative errors was calculated for each patient.^{3,7}

The **Go-Nogo** paradigm was chosen from the Frontal Assessment Battery (FAB¹⁸) to assess patients' ability to inhibit automatic, reflexive behaviour to a distractor. Patients were asked to follow the following instruction: “Tap twice when I tap once. Do not tap when I tap twice”.^{18,19}

The number of errors in the tapping responses during 10 trials was analysed and rated based on the FAB test manual (0 errors=3 points; 1-2 errors=2 points; 2-3 errors=1 point; ≥ 4 errors=0 points).

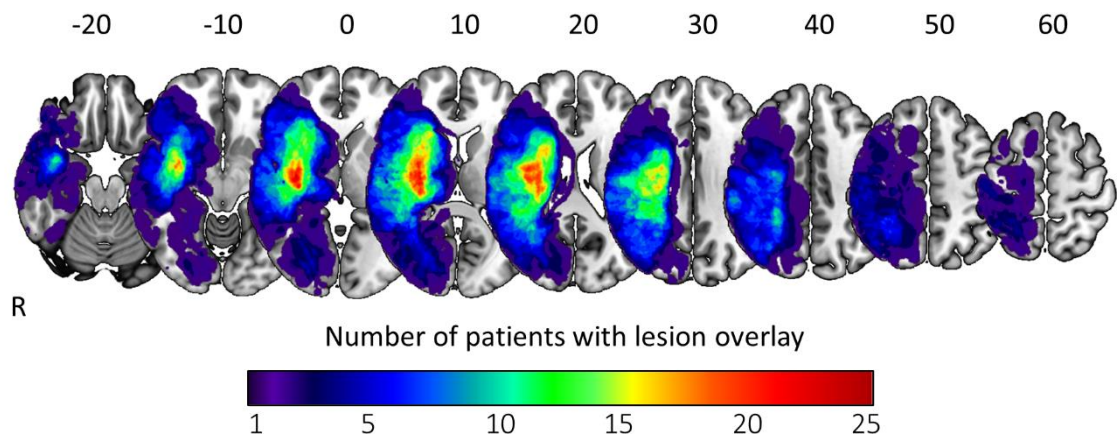
The **Stroop** Colour and Word Test²⁰ was used to assess inhibition as a form of interference suppression (i.e., naming the ink colour of incompatible colour words). We used the Stroop interference test included in the German version of the Delis-Kaplan Executive Function System (D-KEFS²¹), and analysed the individual number of interference errors.

The **antisaccade task** was used to assess patients' ability to inhibit automatic, reflexive saccade towards a peripheral distractor. Hereby, patients were asked to fixate a cross in the centre of the screen. After a pseudo-randomized duration of 2,500 to 3,500 msec, the fixation cross disappeared and a black dot (diameter=0.4° of visual angle) was peripherally presented on the right or the left, at a distance of 10° visual angle from the middle of the screen. The patients were asked to perform a saccade in the opposite direction of the peripheral dot. After a delay of 5000 msec, the peripheral dot extinguished, and the next trial began. Patients performed 4 practice trials (not included in the analysis), followed by 12 testing trials. In the offline analysis, the percentage of inappropriate responses (i.e., saccades towards the visual target) was calculated for each patient.²²

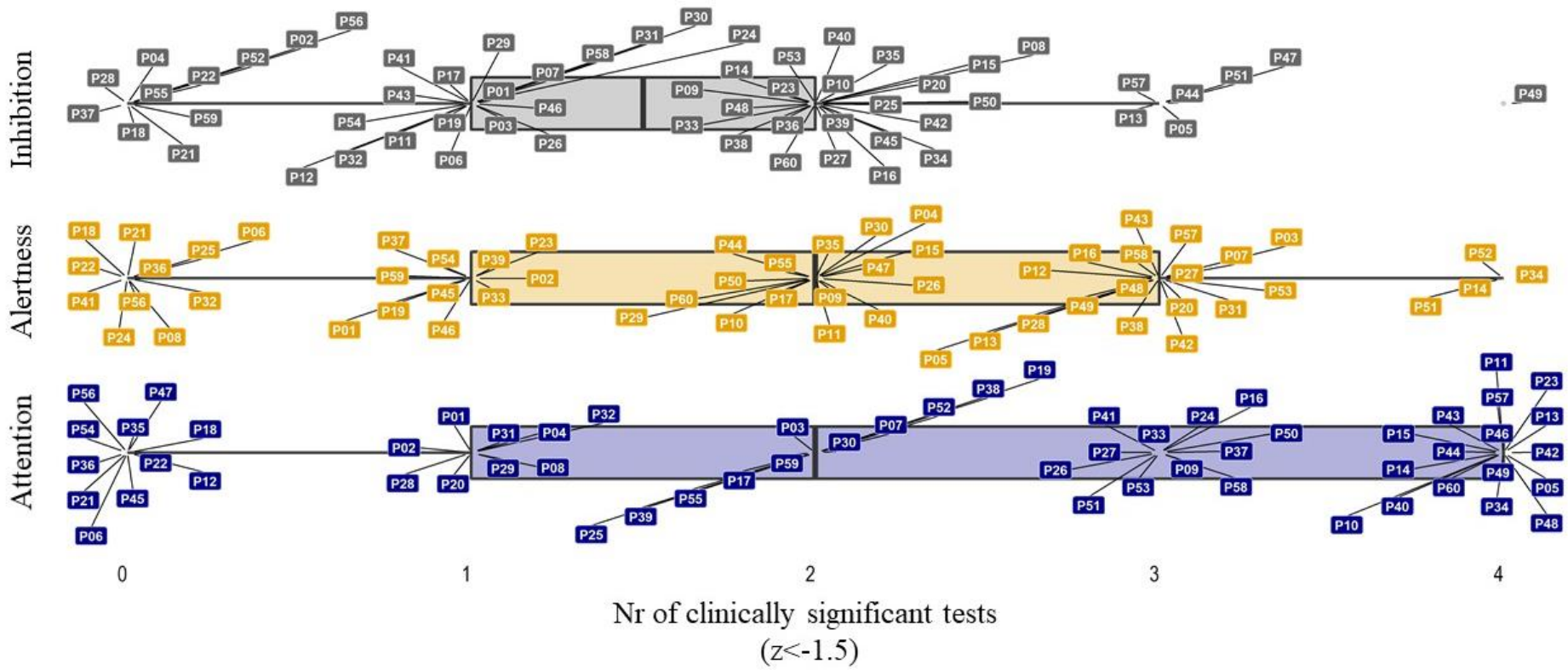
Video-Oculography Apparatus

For all video-oculography measures, eye movement data were recorded as previously described.^{5,10,13} In short, we used a remote, infrared-based video-oculography system (EyeLink 1000Plus System, SR Research; Ottawa, Canada), set to detect saccades in case of an eye movement of at least 0.3°, and either speed exceeding 30°/s or acceleration exceeding 4000°/sec². Prior to the experiment, the video-oculography system was calibrated, and the calibration was validated, by means of 3 × 3-point grids. During the experiment, patients were seated in front of the screen with their head positioned on a chin-and-forehead rest, in order to minimize head movements and to ensure that their mid-sagittal plane was aligned with the middle of the screen (screen size 1400 x 900 pixels), at a constant distance of 67cm (resulting in a visual angle of approximately 34° x 21° visual angle).

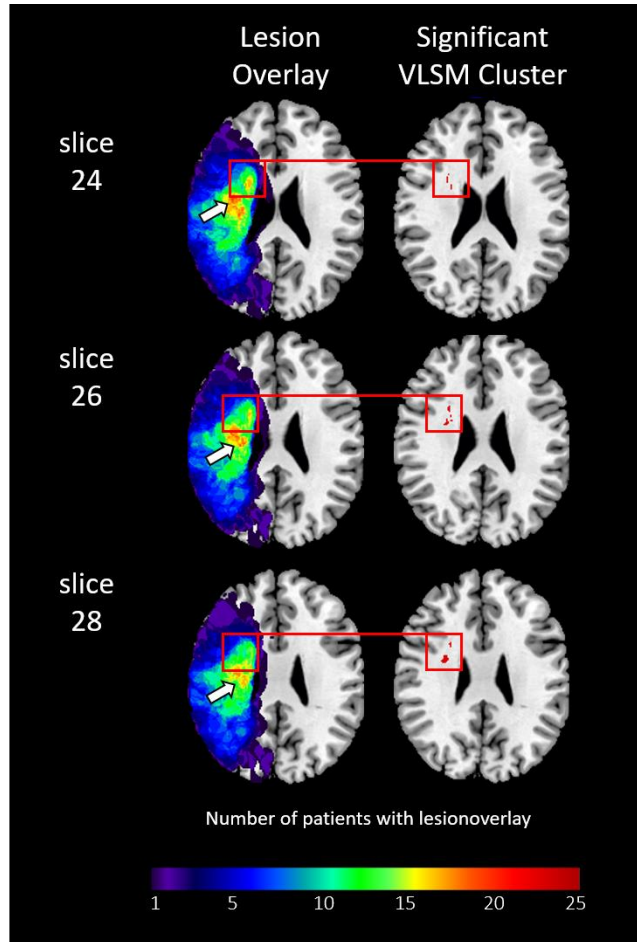
Supplementary Results



Supplementary Figure 1 Lesion overlay for all 60 right-hemispheric stroke patients included in the study. The color-coded legend is determined by the number of patients with damage to a specific brain region. Axial slices are oriented according to the neurological convention. The z-position of each axial slice, in MNI coordinates, is indicated by the numbers at the top of the figure.

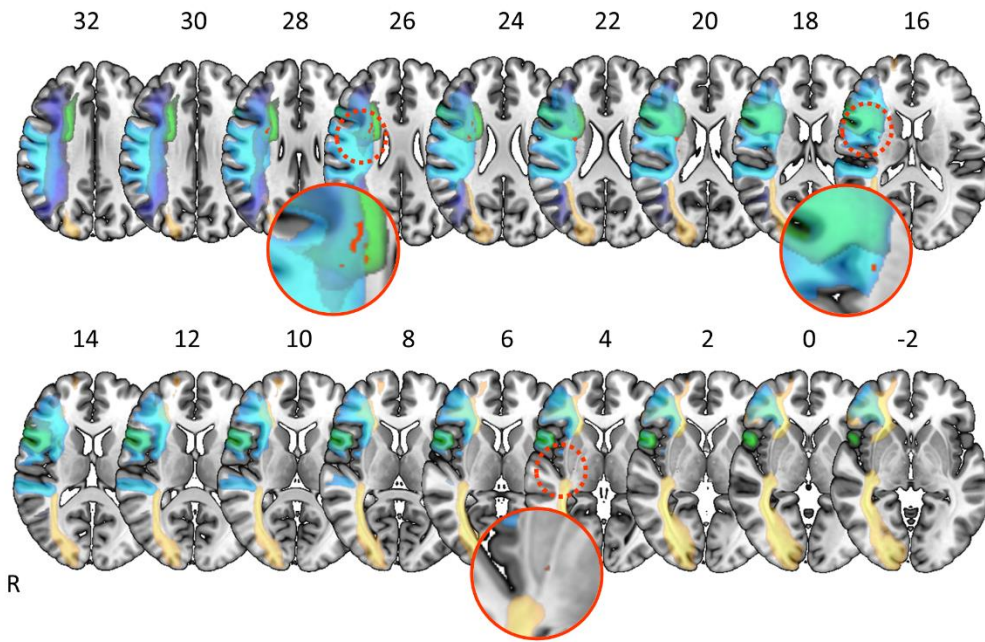


Supplementary Figure 2 Number of clinically significant tests per patient and cognitive domain. The box-and-whisker plots show the number of clinically significant tests per cognitive domain (ranging from 0 i.e., no clinically significant deficits to 4 i.e., clinical significant deficits in all four tests of this cognitive domain): visuospatial attention (blue), alertness (yellow) and inhibition (grey). The individual patients' performance is indicated by means of small rectangles including the patient label. The overall median z-values are indicated by the vertical black line in each box-and-whisker plot. Each box represents the lower (Q1) to the upper (Q3) quartiles, with whiskers extending from the minimum to the maximum of 1.5 times the interquartile range. Outliers are depicted by grey circles.

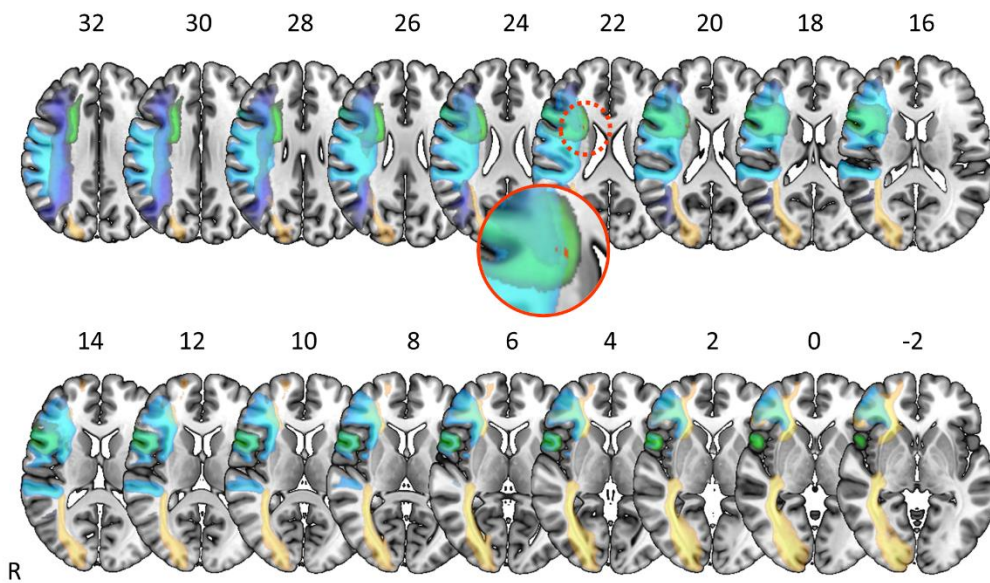


Supplementary Figure 3 Lesion overlay plot (left) compared to the critical cluster identified in the VLSM analyses, lying within the SLFII/III/FAT intersection (right). A comparison of the location of the critical lesion cluster lying within the SLFII/III/FAT intersection (right part of the figure) and the location of the maximum lesion overlap (left part of the figure; the maximum lesion overlay is highlighted by white arrows) shows that these two locations do not match. This speaks against a simple bias in terms of a non-specifically higher frequency of lesions in the area of the identified critical cluster.

A. Letter CoC

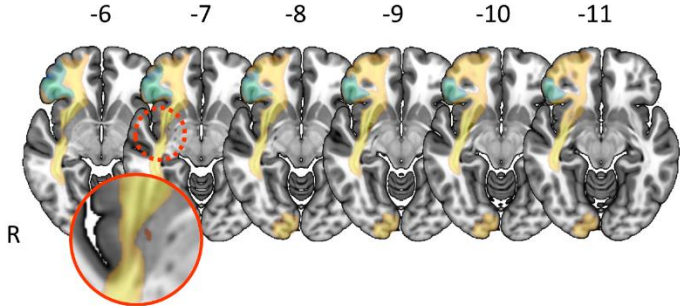


B. Line Bisection

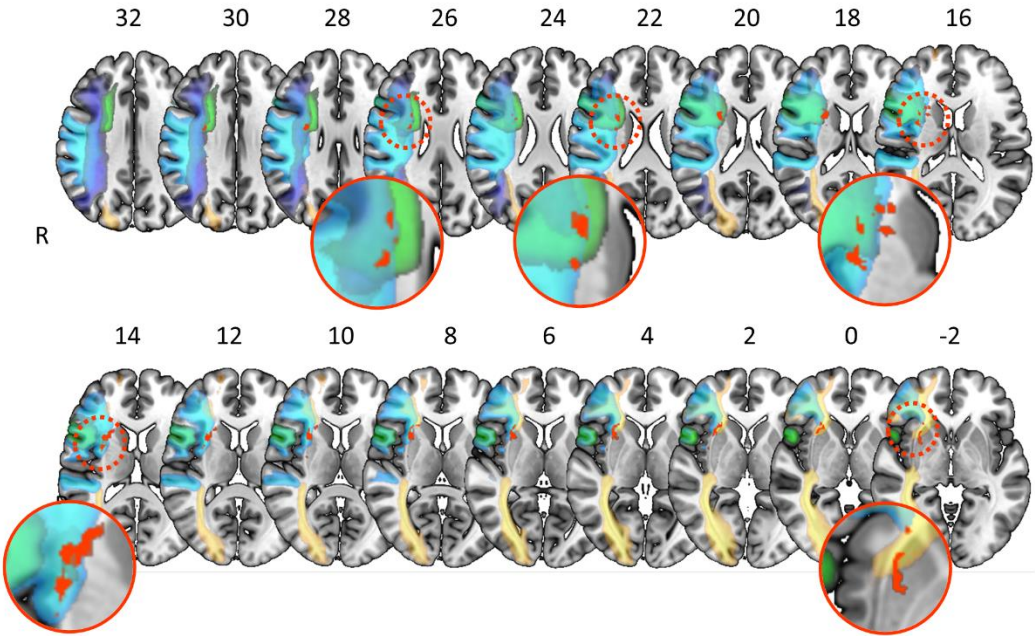


- Superior Longitudinal Fasciculus II (SLF II)
- Superior Longitudinal Fasciculus III (SLF III)
- Frontal Aslant Tract (FAT)
- Inferior Frontal-Occipital Fasciculus (IFOF)

C. Tonic Alertness

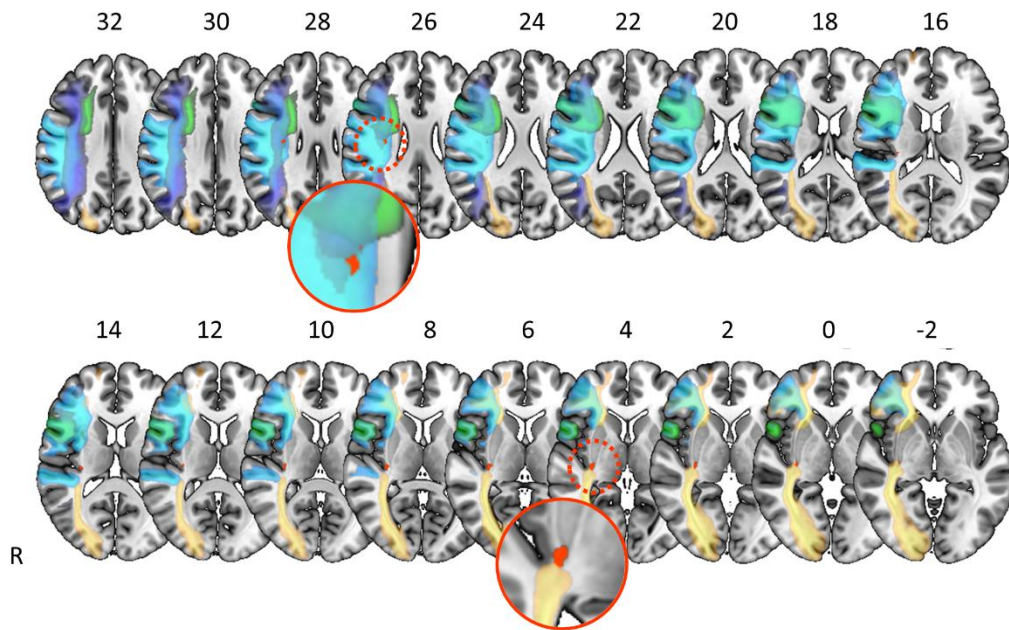


D. Phasic Alertness

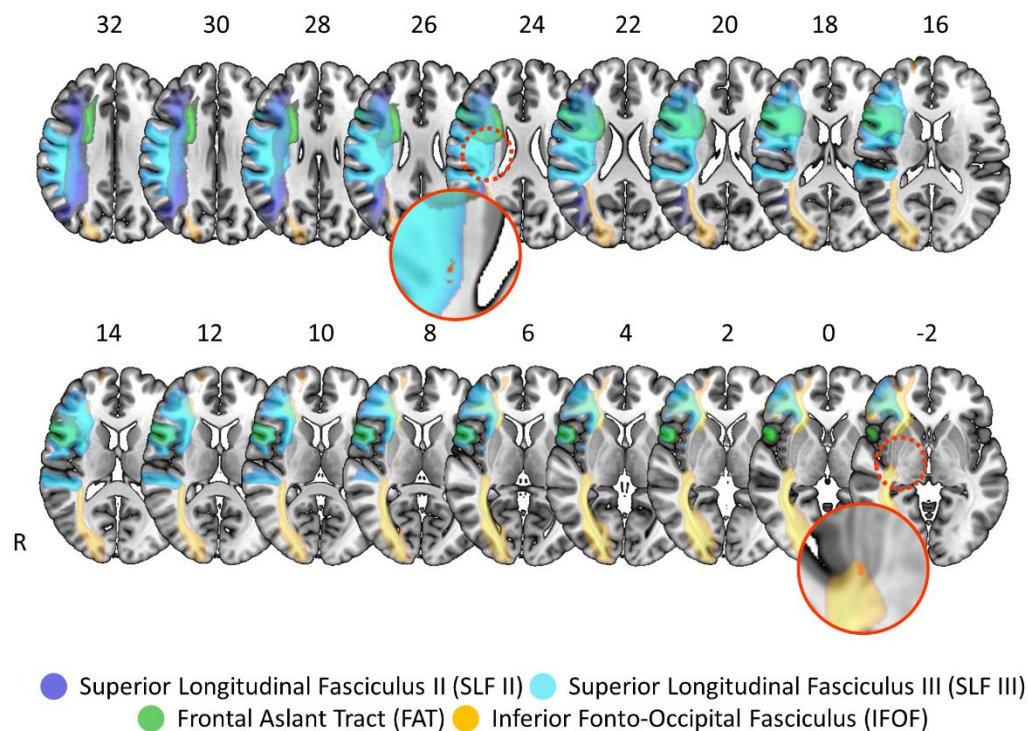


- Superior Longitudinal Fasciculus II (SLF II) ● Superior Longitudinal Fasciculus III (SLF III)
- Frontal Aslant Tract (FAT) ● Inferior Fonto-Occipital Fasciculus (IFOF)

E. Perseverations in the Five-Point Test



F. Go/Nogo



Supplementary Figure 4 Significant results for the additional VLSM analysis for each outcome variable included in the study. (A) Letter CoC depicts the results of the VLSM analysis using the CoC values from the Letter Cancellation test (z-values) as predictive values. The results show two significant lesion clusters (with a total of 241 voxels) within FAT, SLFIII, as well as the SLFII/III/FAT intersection,^{25,26} and in the subthalamic radiation (XTRACT HCP Probabilistic Tract Atlas implemented in FSL) and the IFOF²⁶. (B) Line

Bisection depicts the results of the VLSM analysis using the relative deviation in the Line Bisection Test (z-values) as predictive values. The results show two significant lesion clusters (with a total of 38 voxels) within the FAT and the SLF III.^{25,26} **(C) Tonic Alertness** depicts the results of the VLSM analysis using the median reaction time in the TAP subtest for tonic alertness (z-values) as predictive values. The results show a significant lesion cluster (with a total of 16 voxels) within the Putamen (Harvard Oxford Cortical Structural Atlas implemented in FLS) and at the border of the IFOF²⁶. **(D) Phasic Alertness** depicts the results of the VLSM analysis using the median reaction time in the TAP subtest for the phasic alertness (z-values) as predictive values. The results show two significant lesion clusters (with a total of 158 voxels) within SLF II, FAT as well as the intersection of SLFII/SLFIII/FAT^{25,26} and in the Putamen (MNI Atlas implemented in FSL), the IFOF²⁶ and the insular Cortex (Harvard Oxford Cortical Structural Atlas implemented in FLS) and Caudate (MNI Structural Atlas implemented in FSL). **(E) Perseverations in the Five-Point Test** depicts the results of the VLSM analysis using the FPT Perseverations (z-values) as predictive values. The results show two significant lesion clusters (with a total of 326 voxels) within SLF III, the intersection of SLFII/SLFIII^{25,26} the Putamen (Oxford-Imanova Striatal Structural Atlas implemented in FSL), the Insula (MNI Structural Atlas implemented in FSL), and at the border of the IFOF²⁶. **(F) Go/Nogo** depicts the results of the VLSM analysis using the Go/Nogo (z-values) as predictive values. The results show two significant lesion clusters (with a total of 43 voxels) within the SLF III^{25,26}, the Putamen (Harvard Oxford Cortical Structural Atlas implemented in FLS) and at the border of the IFOF²⁶. Lesion voxels that were a significant predictor for the respective variable are depicted in red (significance level $p < .05$, based on the Brunner-Munzel test, FDR-corrected, 4000 permutations). Lesion clusters and white matter tracts are displayed on the MNI152 template in MNI space, as available in MRICroGL (<https://www.nitrc.org/projects/mricrogl/>). The axial slices are oriented according to the neurological convention. The position of each slice in MNI space is indicated by numbers at the top of the respective slices. SLF II (in dark blue), SLF III (in light blue) and FAT (in green) white matter tracts are depicted according to published probabilistic diffusion tensor imaging tractography atlases^{25,26} (the probability for voxels to belong to the SLF II, SLF III and the FAT was set at $>50\%$, i.e., above chance).

Supplementary Table 1: Summarizing the significant lesion cluster of the VLSM analysis per outcome variable

Cognitive component	Outcome variable	Nr of sig. clusters	Total Nr of Tracts sig. voxels	
Visuospatial Attention	Letter CoC	2	241	SLFII/III/FAT intersection FAT SLFIII subthalamic radiation SLFIII/IFOF
	Line Bisection	1	38	SLFII/III/FAT intersection SLFIII/FAT intersection FAT
Alertness	phasic alertness	2	158	SLFII/III/FAT intersection SLF III/FAT SLF III FAT Putamen Putamen/IFOF Insular Cortex Caudate SLFIII/IFOF IFOF
	tonic alertness	1	16	Putamen Putamen /IFOF
Inhibition	Five-Point Test Perseverations	2	326	SLFII/III/FAT intersection SLFII/III intersection SLF III Putamen Insular Cortex Putamen/IFOF IFOF (border)
	Go/Nogo	2	43	SLF III Putamen Putamen/IFOF (border)

Note. Significant VLSM results were found for a total of six outcome variables from all three cognitive domains; visuospatial attention (Letter Cancellation Tests, Line Bisection Test), alertness (TAP phasic Alertness, TAP tonic Alertness), and inhibition (percentage of perseverative errors in the Five-Point Test, Go-Nogo paradigm of the FAB). Atlases used; ^{25,26} and FSL implemented *Harvard Oxford Cortical Structural Atlas*, *Oxford-Imanova Striatal Structural Atlas*, *MNI Structural Atlas*, *XTRACT HCP Probabilistic Tract Atlas*.

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