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Supplementary Information for:

Post-Stroke Acute Dysexecutive Syndrome, a Disorder Resulting from Minor Stroke due to Disruption of Network Dynamics

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Supplementary Information

Clinical Assessment:
All subjects were administered the Montreal Cognitive Assessment (MoCA) and modified Rankin Scale (mRS) at the time of each MEG visit, approximately 6 months apart. Individual results for each time point are reported below (Tables S1 and S2).

Magnetoencephalography Analysis:
All subjects were scanned at visit 1 and visit 2 using a 157-channel whole-head MEG system (KIT-Eagle Technology, Kanazawa Japan). The scanner is used for research purposes only, and does not currently have the capability to record simultaneous EEG or routinely perform biocalibration (e.g., using simple auditory or visual stimuli to ensure consistent placement within the scanner). Proposals are under way for these features to be available for future research protocols to further improve our quality assurance practices.

Marker Measurement and Head Shape Digitization
Prior to the recording, each subject's head shape was digitized using 3 fiducials and 5 marker positions. A hand-held electronic stylus (part of the Polhemus 3SPACE FASTRAK system) was used to record the position of approximately 1,000-2,000 points on the scalp and face surface in 3d space. This process involves sitting still for 10 to 30 minutes while the stylus is rubbed across the scalp. The resulting 3d head model was used to co-register the subject's head shape with the Freesurfer "fsaverage" brain[1] using rotation, translation, and uniform scaling. Five coils were then attached to the head (one at each marker point) to localize head position relative to the MEG sensors during analysis. During the recording session, the subject was asked to place their head as deeply into the scanner helmet as possible, until they could feel it touching the top. Formal marker measurements were obtained at the beginning and end of each task. During MEG data processing (below), pre- and post-marker measurements were compared using the kit2fiff GUI tool used to quantify minor head movement during the task, and the average measurement was used in further analyses. Movement for all subjects was fortunately minimal.

Pre-Processing
The raw data were visually inspected using the scanner manufacturer provided software by an independent reviewer (RHL) trained in EEG, for abnormal activity including spikes, sharp waves, and seizure activity in both patients and controls. None was observed.

Data Processing
MEG data were processed using the Eelbrain 0.31.7[2] and MNE-Python 0.19.0 software packages.[3,4] For each task, raw data were first converted to .fif files, accounting for potential movement during the task as described above, using the kit2fiff GUI tool. Flat and noisy channels were then excluded, and data were band-pass filtered between 1 - 40 Hz using a zero-phase FIR-filter within the MNE-Python default settings. Next, Independent Component Analysis (ICA) was applied. Components were estimated using the extended infomax algorithm after reducing the dimensionality of the input data to a number of PCA components explaining 99% of the variance (this dimensionality reduction was only applied for estimating ICA components and not for further analysis). By visual inspection, components reflecting biological artifacts (heartbeats, saccades, and eye blinks) were removed. Data epochs were then extracted from -100-1000 ms relative to stimulus onset for the presentation of words or images, and downsampled to 200 Hz. Epochs with recording artifacts were removed by visual inspection, along with trials with reaction times of greater than 2 standard deviations above the subject's individual mean for that task, in order to exclude potential outliers. The remaining epochs were averaged to estimate the response to images and words independently for each participant.

Analysis
Sensor RMS- Our analysis included the use of RMS to summarize responses across sensors and compare response magnitude between stroke patients and controls. Following data processing

(described above), all epochs within the Visual Task (Familiarization, Match Mismatch, Pairs Naming, and Pairs Description) for each participant were loaded for visits 1 and 2. Time series were analyzed using cluster-based permutation tests at each time point between 50-600 ms following the presentation of either images or words (analyzed separately). This period was chosen given our pre-determined peaks of interest. An average activation pattern was calculated in response to images and words for each group, and patterns were compared between groups using independent t-tests for each visit. Paired t-tests compared results across visits for the participants in each group who underwent repeat imaging (n=6 patients, 6 controls). Significant differences were found between stroke patients and controls at both visits. On visual inspection, there appeared to be a change within stroke patients from visit 1 to visit 2, with increasing amplitude, while controls remained consistent; however, this was not statistically significant. This may be due to our relatively small sample size.

RMS can be sensitive to head size and location within the scanner, a limitation of this type of analysis; however, stroke patients consistently demonstrated lower amplitude levels of activation compared to controls, and this was consistent between visits 1 and 2 which argues against accidental positioning differences. Future studies would benefit from an objective biocalibration to monitor consistency of placement between groups.

Source Localization- The digitized headshape was fitted to the Freesurfer "fsaverage" template head using the MNE-Python coregistration GUI tool. The head models were first aligned using the 5 markers, then scaled and aligned using the other data points obtained from the digitized headshape. The Desikan atlas was then used to create areas of interest by combining "aparc" labels to create the following areas: occipital lobe (pericalcarine fissure, cuneus, lateral occipital lobe), fusiform gyrus (fusiform), and lateral temporal lobe (superior, middle, inferior, and transverse temporal gyri, superior temporal sulcus, temporal pole). These areas were chosen based on our interest in the early visual, word form, and semantic processing responses. The expected peaks were confirmed within each of these areas using overlay plots (manuscript Figure 1). Activity, time-locked to the events of interest (image or word presentation) was source-localized using dSPM, or distributed norm estimates, normalizing the current estimate by the variance of the noise estimate, similar to the creation of a Z-score.[5] Within our pre-defined areas of interest, spatio-temporal cluster-based permutation tests were used to detect significant effects and time courses were visualized in regions of interest based on significant clusters. Large clusters (based on positive F-values) often combined regions with positive and negative (signed) current direction due to varying cortical folding. This was accounted for in the following manner:

Fusiform gyrus. Within the fusiform gyrus, we were able to evaluate selected clusters with constant orientation by separating the data into anterior and posterior fusiform regions. Data were evaluated between 150-400 ms, to best capture the M170 response. Representative clusters of the left anterior and posterior fusiform gyrus were chosen for display within Figure 4, but all significant clusters are included in Table 2.

Lateral temporal lobe. Within the temporal lobe, we had to account for the fact that clusters often spanned multiple gyri. Consequently, a dominant upward current might appear as positive current on the upper wall, and negative current on the lower wall of the gyrus. A common solution to this issue is "sign flipping" some of the currents to make the currents consistent for averaging. Here, since the dominant current estimate was vertical, we used the vertical orientation of the current dipole to determine which currents to flip. We flipped the currents from all dipoles whose vertical orientation was negative (i.e., all downward-pointing dipoles). After this sign flipping step, the ROI signal was determined by averaging as for the other ROIs. A time period of 300-600 ms was used to best capture the M400 response.

Similar to RMS analysis, groups were compared using independent t-tests at each visit, and paired t-tests were used to compare changes within groups across visit 1 and visit 2. In all cases, averaging was used rather than the maximum waveform given that it represents a more conservative approach. Using the maximum waveform would be prone to being overly affected by outliers. While using the average may diminish the magnitude of the observed effect, it increases SNR by aggregating across multiple data points.

Task-Specific Modulation- To evaluate the effect of task difficulty on modulation of cerebral activation, we focused on the response to words within our 3 pre-defined areas of interest. The visual task was broken down into its subtasks (Familiarization, Match Mismatch, Pairs Naming, and Pairs Description). Time courses were plotted within each ROI for patients versus controls at visit 1 and 2. ANOVA was used to evaluate task by group interactions at each visit.

Table S1. Individual Participant Performance on Cognitive Testing at Visit 1 and Visit 2. Note that controls tended to remain consistent over time, while stroke patients were initially more impaired and then often improved their scores between visits.

					Visit 1							**Visit 2**						
	Age	*Sex*	*Race*	*Level of Education*	*Barthel Index*	*NIHSS*	*mRS*	*MOCA*	*F Letters*	*S Letters*	*Boys Names*	*Barthel Index*	*NIHSS*	*mRS*	*MOCA*	*F Letters*	*S Letters*	*Boys Names*
control	47	F	W	masters	100	0	0	30	15	10	19	100	0	0	30	19	20	25
control	67	F	B	2 years of college	100	0	0	29	11	17	20	100	0	0	25	13	17	29
control	42	F	W	masters	100	0	0	30	11	17	23	100	0	0	30	17	18	19
control	71	M	W	bachelors	100	0	0	26	9	15	18	100	0	0	29	11	12	19
control	51	M	W	PhD	100	0	0	30	20	18	22	100	0	0	30	22	28	24
control	53	M	W	medical school	100	0	0	28	14	12	14	100	0	0	29	17	15	19
control	53	M	W	medical school	100	0	0	30	18	16	21							
control	80	F	B	bachelors	100	0	0	26	19	20	22							
stroke	43	F	W	masters	100	0	1	24	13	9	13	100	0	1	26	13	17	27
stroke	80	M	W	bachelors	100	0	1	26	20	23	28	100	0	0	27	30	26	31
stroke	76	M	W	7th grade	100	3	1	21	8	9	9	100	0	1	20	9	8	9
stroke	56	F	B	12th grade	100	2	1	24	14	12	15	100	0	0	29	10	11	21
stroke	66	F	W	12th grade	100	0	0	28	12	16	15	100	1	1	30	16	15	18
stroke	37	M	B	12th grade	100	0	1	28	12	9	19	100	0	0	27			
stroke	47	M	B	12th grade	100	0	1	28	11	18	18							
stroke	57	F	B	PhD	100	1	2	22										
stroke	76	F	W	nursing school	100	0	1	27	23	30	31							

Visit 1- approximately 1 month post-stroke; Visit 2- approximately 6 months post-stroke

NIHSS (National Institutes of Health Stroke Scale); mRS (modified Rankin Scale); MOCA (Montreal Cognitive Assessment)

**Sex (F= female, M= male)*

***Race (W= white, B= black)*

Table S2. Mean Individual Participant Times (in seconds) on the Visual Matching Tasks. Note that stroke patients tended to take longer to respond and make more errors than controls at both visits. Both groups demonstrated faster reaction times at visit 2.

	Visit 1						Visit 2					
	Match Mismatch Time	*Match Mismatch Incorrect*	*Pairs Naming Time*	*Pairs Naming Incorrect*	*Pairs Description Time*	*Pairs Description Incorrect*	*Match Mismatch Time*	*Match Mismatch Incorrect*	*Pairs Naming Time*	*Pairs Naming Incorrect*	*Pairs Description Time*	*Pairs Description Incorrect*
control			1.0510	0	0.9434	1	0.6099	0	0.6902	0	0.9098	0
control	1.2802	0	1.2351	2	1.7560	2	1.7762	1	0.8797	2	1.0299	1
control	0.5550	1	0.6871	0	0.8235	1	0.5671	2	0.5937	0	0.7402	3
control	0.6439	0	0.8385	1	1.1627	3	0.7855	1	0.9202	0	1.3177	1
control	0.5727	2	0.6015	0	0.7579	1	0.5320	1	0.6067	0	0.7354	1
control	0.6630	1	0.7204	0	1.0919	3	0.8203	0	0.7715	1	0.9904	1
control	0.6346	1	0.8125	0	1.0782	1						
control	0.8475	1	2.2728	2	1.6978	1						
stroke	0.7690	1	1.0461	0	1.2880	1	0.6852	0	0.8392	0	1.1403	1
stroke	0.6037	2	0.9600	1	1.1457	3	0.7418	3	0.8249	4	1.1001	5
stroke	6.7550	5	2.4390	5	7.8990	11	2.3123	6	1.9478	23	2.8724	24
stroke	0.7160	1	1.6131	5	1.7546	4	0.7509	1	1.0239	4	1.4550	3
stroke	1.0761	0	1.5231	0	1.6193	2	0.8950	2	1.3415	3	1.7715	3
stroke	3.5715	13	4.8260	8	4.6849	3	0.6260	1	0.6934	2	0.9995	1
stroke	0.8199	1	0.8097	2	1.2411	2						
stroke	1.5673	5	2.0011	2	1.8944	3						
stroke	0.8148	4	0.9654	0	1.1055	3						

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