BONeS not CATs attract DOGS: Semantic context effects for picture naming in the lesioned language network.

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Short Title:

Semantic context effects after brain lesion.

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Abstract

The breakdown of rapid and accurate retrieval of words is a hallmark of aphasic speech and a prime target of therapeutic intervention. Complementary, psycho- and neurolinguistic research have developed a spectrum of models, how and by which neuronal network uncompromised speakers can rely on remarkable lexical retrieval capacities. Motivated by both lines of research we invited 32 participants with a chronic left hemispheric brain lesion to name pictures in the presence of distractor words. This picture-word-interference (PWI) paradigm is widely used in psycho- and neurolinguistic research.

We find that also after brain lesion categorically related words (CAT → [dog]^{picture}) impede naming, while a associatively related words (BONE → [dog]^{picture}) ease access. The effects largely affecting latencies in neurotypical populations, are reproduced for error rate in our participants with lesions in the language network. Unsurprisingly, overall naming abilities varied greatly across patients. Notably, however, the two effects (categorical interference / associative facilitation) dissociate between participants. Correlating performance with lesion patterns we moreover find robust evidence for a dissociation of brain areas affording different aspects of the task: (i) lesions in the left MTG deteriorate overall naming, confirming previous work; more notably (ii) lesions comprising the inferior frontal hub of the language-network increase interference effect for the categorical condition; on the contrary (iii) lesions to the mid-to-posterior temporal hub increase the facilitatory effect for the associative condition on error rates.

The findings are of relevance to the understanding of the functional anatomy of word-retrieval. Although experimental in nature the data moreover suggest that depending on lesion site different strategies may be required in the rehabilitation of aphasic word retrieval deficits.

Keywords: Semantic Interference, Picture word interference paradigm, Aphasia, Stroke: imaging, Cortical plasticity, Stroke: rehabilitation, Temporal lobe, Frontal lobe

1. Introduction

Rapid and accurate lexical retrieval is a prerequisite for fluent language production. The ease by which we choose the correct word from the large mental lexicon is, however, brittle: errors occur in uncompromised speakers, increase with normal ageing (Meinzer et al., 2009, Bortfeld et al., 2001) and may be an early sign of imminent cognitive impairment (Mueller et al., 2017). Moreover, word finding difficulties are the most common deficits persisting in aphasia, even if residual (Kohn and Goodglass, 1985). Research on the mechanisms underlying lexical retrieval has identified a number of factors modulating its speed and accuracy. Unsurprisingly, lexical frequency is relevant: retrieval of the word ‘flamingo’ is harder than ‘duck’. However, in the sentence ‘On the safari she most liked the sight of a lake crowded by pink___’ the frequency advantage for ‘duck’ is overridden by context. It seems intuitive that a specific semantic context should ease retrieval of semantically related words. However, there is abundant evidence for semantic-categorically related context words to interfere with the naming response of the target ($\text{cat}^{\text{context}} \rightarrow \text{dog}^{\text{target}}$). In fact, competition within a lexical cohort is a key feature of a classical model for word production (Levelt et al., 1999, Roelofs, 1992). It posits that successful retrieval of a member of the cohort (e.g. ‘animals’) is more time consuming and error prone, the higher the activation of other category-members. This may result from a relative selection threshold to be surpassed (e.g. Levelt et al., 1999) or from lateral inhibition between co-activated representations (e.g. Harley, 1993)). Therefore, retrieval of ‘dog’ is hampered by the co-activation of ‘cat’ but not ‘car’. Moreover, ‘cat’ is the more likely erroneous output, when the intended word ‘dog’ cannot be retrieved, as evidenced by semantic errors in aphasic speech (Schwartz, 2014).

Competition in word production is supported by numerous studies demonstrating semantic interference from categorically related contexts. Three principal designs with several variations have been used. Blocked-Cyclic and Continuous Naming require naming of pictures in

succession. Interference is evidenced in that reoccurrence of a specific category (e.g. animals) increases naming latency for a successive exemplar of that category in Continuous Naming (e.g. Oppenheim et al., 2010)). Similarly, blocks with categorically related items presented repeatedly slow naming compared to unrelated item blocks (e.g. Kroll and Stewart, 1994, Damian et al., 2001). The other widely used paradigm is the Stroop-like picture word interference paradigm (PWI) in which speed and accuracy of picture naming is assessed in the context of a distractor word (Glaser and Dungelhoff, 1984)¹. Again *categorically* related words interfere with the naming of the target picture when compared to a semantically unrelated word. Conversely, in PWI paradigms associatively related context words (bone^{context} → dog^{target}) have been shown to facilitate naming (La Heij et al., 1990). Neurotypical participants name the picture of a dog faster when the word ‘bone’ has been presented prior to the picture, when compared to an unrelated word.

The locus at which interference impacts on production is controversial. In the above model the *lexical* level of word production is considered to be sensitive to interference (Roelofs, 1992, La Heij, 1988, Damian and Bowers, 2003), while at the conceptual level semantic relatedness elicits facilitation (Bloem and La Heij, 2003). Since verbal competitors induce *facilitation* when presented 400 ms prior to the target, the model additionally posits that lexical competition decays faster than conceptual facilitation (Bloem et al., 2004). However, in word-picture matching tasks, not requiring lexicalization of the competitors, semantic interference effects have been shown also in neurotypical participants (Harvey and Schnur, 2016, Campanella and Shallice, 2011). This suggests a *prelexical* locus of interference in the semantic system. To explain semantic interference in continuous naming and blocked cyclic naming paradigms incremental learning mechanisms, strengthening the connection between semantic and lexical representations have been suggested (Belke and Stielow, 2013, Oppenheim et al., 2010). To

¹ The design resembles Stroop paradigms requiring the suppression of a written distractor. For a discussion on the similarity and differences between tasks, see Starreveld & La Heij 2017.

complicate matters, semantic interference in the PWI task has also been ascribed to control processes operating at *postlexical* stages of word production (Finkbeiner and Caramazza, 2006, Mahon et al., 2007). One motivation for this is the finding that frequency effects of the distractor words are inverse to what is expected for lexical competition² (Dhooge and Hartsuiker, 2011, cf. Roelofs et al., 2011). Models postulating a lexical versus postlexical level of interference may not be mutually exclusive. An elegant fMRI study demonstrated differential effects of distractor word's *frequency* versus its *age-of-acquisition*. While frequency modulated brain activation in areas putatively affording postlexical processes (bilateral premotor / left pSTG/pMTG) age-of-acquisition modulated activation in areas assumed to house the lexicon (mostly left mid-MTG). Thus interference at different stages of the naming process may be assumed (de Zubicaray et al., 2012).

Another controversial issue regarding semantic interference effects pertains to the question how activation of a lexical cohort, competition between cohort members and selection of the target interact. Differences between high versus low demand scenarios and varying task requirements have provided evidence for competitive (Roelofs, 1992) but also non-competitive (Mahon et al., 2007) accounts. Of special relevance to the present study, this issue extends to the question in how far lesions to the language network can differentially alter activation and selection processes resulting in non-fluent and/or erroneous production in people with aphasia (Nozari and Hepner, 2019, Anders et al., 2017, Ries et al., 2019). Beyond their role in shaping models of word production, semantic context effects during picture naming are of relevance to interventions in people with aphasia, since various confrontational naming schemes may be considered a pillar of Speech-and-Language-Therapy (SLT, e.g. Conroy et al., 2018).

² High frequency (HF) show smaller interference effects when compared to low frequency (LF) distractors. This contradicts the lexical competition account in that higher intrinsic activation level of HF-words should increase interference.

To address these issues we here investigate in how far facilitation and interference can be elicited in the lesioned language network and whether either process relates to dissociable processes corresponding to dissociable ‘hubs’ in the neuronal network affording confrontational naming. Using a well-controlled set of word-picture pairs (Henseler et al., 2014) in participants with circumscribed chronic lesions in the left-hemispheric language network, we hypothesized that interference and facilitation effects are respectively modulated by lesions in distinct parts of the network. Following a parsimonious approach to levels of speech production (Nozari, 2021) we focus on two stages of lexical retrieval: *activation* of the lexical cohort and *selection* of the lexical entry. We hypothesize lesions in areas housing the lexicon to alter lexical (cohort) activation, which should differ from the effect of lesions in brain areas affording lexical selection. While it is uncontroversial, that a distributed network supports lexical retrieval, evidence from neurotypical participants (Binder et al., 2009, Maess et al., 2002, de Zubicaray et al., 2001) and lesion studies (Schwartz et al., 2009, Baldo et al., 2013) converges on lexical activation to rely on the left middle/inferior temporal gyrus (MTG/ITG). Regarding lexico-semantic selection processes especially under higher demand conditions frontal areas including the left IFG have been suggested of relevance (Schnur et al., 2009, Abel et al., 2009, Badre et al., 2005). However, the role of left frontal areas in semantic interference is more controversial. For example participants with lesions of the lateral prefrontal cortex (PFC) showed no increase in interference for semantic cohort distractors in a PWI paradigm, while overall lexical interference (all lexical vs. non-lexical distractors) was augmented (Piai et al., 2015, Piai and Knight, 2018).

The current work is the first lesion study to directly compare categorical interference and associative facilitation in a PWI paradigm in a larger group of patients; therefore functional anatomic hypotheses remain tentative. We predict (i) lesions in frontal areas relevant for *selection* to increase interference effects elicited by categorically related primes (Anders et al., 2017) while (ii) lesions in areas housing the lexicon should reduce target and cohort activation.

Reduced cohort and target activation may increase categorical interference due to “noisy access to lexical representations” (Harvey and Schnur, 2015). However, associative priming may conversely become more relevant supporting the selection process, since overt behavioral effects represent the net of underlying competitive and facilitatory processes (Abdel Rahman and Melinger, 2019, van Scherpenberg et al., 2020). In sum we expect modulations caused by distinct lesion patterns to interact differentially with lexical competition, prevailing in categorical distractors ($CAT \rightarrow [dog]^{picture}$), and with associative facilitation when the distractor word and the to-be-named picture share an associative semantic relation ($BONE \rightarrow [dog]^{picture}$).

2. Material and Methods

2.1. Participants

32 patients with a chronic, acquired left hemispheric brain lesion participated in the study (age: $mean \pm SD = 51.9 \pm 11.51$ years, [range: 25-76], 16 females). The aetiologies comprised vascular but also other CNS-diseases leading to a circumscribed brain lesion (see **supplemental table ST1**). Patients were selected from a data bank of the Clinic for Cognitive Neurology (University-Hospital Leipzig) and the Max-Planck-Institute for Human Cognitive and Brain Sciences. Exclusion criteria were additional right-hemispheric lesions and severe overall cognitive impairment. Additional cognitive impairments were rated based on a detailed assessment of experienced neuropsychologists to exclude severe attentional, overarching memory and executive deficits. Aphasia was diagnosed based on the standard German assessment battery (Aachener Aphasia Test, AAT, Huber et al., 1984); patients with residual or no aphasia at the time of inclusion had all been documented to show an aphasic deficit at an earlier stage of the disease (**supplemental table ST1** for demographic and clinical information). Regarding language competence, severe naming disorder (subtest naming AAT, $PR < 32$),

dyslexia (subtest written language AAT, PR < 30) or inability to understand the instructions precluded from participation.

In all patients brain imaging allowed for lesion delineation. In 30 patients a high-resolution structural MRI acquired at the MPI-CBS was available (3T Scanner; T1 MP-Rage/mdeft with 1 mm³ isovoxel; FLAIR image as reference). In two patients clinically motivated MRIs, with a lesser resolution were used. All patients gave informed consent according to the Declaration of Helsinki. The experiment was approved by the local ethic committee of the University of Leipzig (Nr.:144/18-ek, 13.4.2018).

2.2. Stimuli

For the PWI-task patients were asked to name a target picture as fast and accurate as possible. A visual distractor word was presented shortly prior to the to-be-named target picture. The semantic relation between word and picture-target differed, resulting in 4 conditions:

- (1) ASS^{related} - associatively related pairs (e.g., Knochen [bone] – Hund [dog])
- (2) CAT^{related} - categorically related pairs (e.g., Kirsche [cherry] – Apfel [apple])
- (3) ASS^{unrelated} - unrelated controls for ASS^{related} (e.g., Reiter [horseman] – Hund [dog])
- (4) CAT^{unrelated} - unrelated controls for CAT^{related} (e.g., Wippe [seesaw] – Apfel [apple]).

There was no overlap of the material (words and pictures) between the associative and categorical conditions. However, the control conditions, (ASS^{unrelated}/CAT^{unrelated}) were created by rearranging the respective set of ASS^{related} and CAT^{related}, abolishing the relationship between picture and word. A fixed delay of -300 ms between word and picture presentation (stimulus-onset-asynchrony, SOA) was used for the associative conditions. For the categorical conditions an SOA of -100 ms was used (**Figure 1A**). These SOAs as well as the two item sets are the same as in Henseler *et al.* (2014) and were chosen to maximize facilitation and interference effects respectively.

The stimulus set comprised 88 black-and-white drawings of everyday objects (40 for categorical, 40 for associative condition, 8 practice items) and the assigned distractor words (set identical to study in neurotypical participants, Henseler et al., 2014). All pictures had high naming agreement in neurotypical participants. Picture sets used in the associative and categorical conditions were matched for linguistic parameters influencing speed of picture naming and distractor recognition, including word length, lemma frequency, name-, image-agreement, visual complexity, familiarity, number of syllables, and graphemes (Henseler et al., 2014, table 1, p.1406). Associatively related distractor words were selected on the basis of an association data base (Melinger and Weber, 2006). Categorically related distractor words were drawn from the same semantic category as the picture names.

2.3. Procedure

The experimental session comprised: consent and instruction, familiarization, training, main experiment, and assessment of reading comprehension.

During *familiarization* participants named all pictures twice, first in the presence of its name written below the picture, then in isolation. To introduce the PWI paradigm, patients were asked to name eight practice items in the presence of unrelated distractors. The *main experiment* required the naming of 80 target pictures. Each picture was named twice: once in the presence of an associatively or categorically related distractor word and once with an unrelated distractor word. To avoid predictions about the following items based on the differing SOAs ASS and CAT conditions were blocked, and presented in blocks of 21 items. The 1st item of each block did not enter analyses since it was used as practice item. ASS and CAT blocks alternated, with their sequence being balanced across participants. Within the eight blocks (four associative/ four categorical) related and unrelated pairs were pseudorandomized. No picture appeared twice within the same block. To avoid sequence effects, related and unrelated conditions for each target picture were counterbalanced across participants. Upon request participants were allowed

pauses between blocks. In all, there were 168 experimental trials per patient (including the eight practice items, one at the beginning of each block).

Because *reading comprehension* of the distractor words is mandatory for the paradigm to work, the ability to access the semantic system via reading was assessed after the main experiment in a word-picture-matching task using the experimental picture set. Despite the lesions in the language network all participants performed at ceiling achieving over 98% correct reactions.

Each trial started with the presentation of a fixation cross for 700 ms followed by a blank screen for 2000 ms. Next the distractor word appeared in the centre of the screen (font: Arial, bold, upper-/ lower-case letters according to German orthography). Picture presentation followed after 100 ms for categorical and 300 ms for associative conditions. The distractor word remained in the centre of the target picture (7 x 7 cm). Presentation ended 3000 ms after the voicekey had been triggered. The response interval started at picture onset, time-out for the response was 10 seconds. The trial structure is illustrated in **Figure 1A**.

The paradigm was implemented on DMDX (Version 5.134). Patients were seated in front of a TFT monitor (Samsung Sync Master 2233R2, 22 inch, 1680 x 1050 pixels) with a viewing distance of ~100 cm. Naming latencies were collected on-line by using a SONY Condenser C-48 microphone and a Nesubox-Lite hardware voicekey. In addition, the experimental sessions were digitally recorded to allow for an off-line validation of speech onset measurements.

Figure 1: (A) Picture-word Interference (PWI) paradigm. A fixation cross was followed by the distractor word in the associative condition (ASS; SOA of 300 ms, ‘Knochen’ *engl.*: bone) and the categorical condition (CAT; SOA of 100 ms, ‘Kirsche’ *engl.*: cherry). The distractor word remained on the screen during target presentation. After the voicekey was triggered the picture remained on the screen for another 3 s. Time-out for the voice key trigger was 10 s. The time window to initiate a response was maximally 10 sec. **(B)** Lesion overlay map of the 32 patients. Coloured areas are lesioned in at least one patient. Lesion-behaviour analyses were performed in areas in which at least 3 lesions overlapped. A more detailed representation of the lesion coverage is supplied in *Supplementary Figure SF1*.

2.4. Statistical analyses

Naming latencies (LAT) and error rates (ERR) were analysed separately. For error analysis the following reactions were coded as errors and discarded from the analysis of latencies: (1) no response, (2) self-corrections, (3) semantic substitutions/paraphasias, (4) phonological substitutions/paraphasias, and (5) reading of the distractor word. Because a number of patients showed word finding difficulties as indicated by filled/unfilled pauses and search behaviour on initial phonemes or syllables due to apraxia of speech or a phonological disorder, the latency analyses required a finer grained off-line analysis. Using the audio recordings and the program Check Vocal (Protopas, 2007), we identified the first complete utterance and used it for adjusting the response-onset measurement. Therefore, hesitations were captured as prolonged naming latency rather than contributing to the error analysis. If an erroneous reaction was interrupted to then produce a correct reaction, this was considered an error. In case of phonetic errors due to dysarthria or apraxia of speech, a reaction was considered correct if at least 75% of the phonemes were correct. For the analyses, these offline determined latencies and errors were used.

Behavioral data (LAT, ERR) were analyzed separately for the associate and categorical conditions. We do not report an overall analysis of relatedness (all related vs. all unrelated items) because the factor “type of relation” (TYPE in the following) was confounded with SOA and with the use of different item sets. To compare associatively / categorically related and their

corresponding unrelated conditions two paired t-tests were conducted (95% confidence interval). Statistical analyses were performed in R (3.3.2).

If associative facilitation and categorical interference can be demonstrated on the group level a central question is whether the two effects dissociate across participants. Therefore we performed several correlation analyses between the effects for overall performance and associative facilitation / semantic interference effects using Pearson's correlation analysis. Moreover, we argue that if the two processes are (partially) independent they may rely on the integrity of partially discernible anatomical hubs in the language network. Therefore, we performed a lesion-behaviour analysis as detailed next.

2.5. Lesion-behaviour analyses

For lesion-behavior analyses, lesions were manually delineated on each slice of the T1-images using MRICron (Rorden and Brett, 2000). FLAIR-images served as a reference. For normalization and transformation of the lesion masks into standard stereotactic space (MNI) the 'clinical toolbox' (www.nitrc.org/projects/clinicaltbx/) in SPM8 (fil.ion.ucl.ac.uk/spm) was used. It applies the unified segmentation approach (Ashburner and Friston, 2005) restricting estimation of normalization parameters to healthy tissue (Brett et al., 2001). Because the resolution of the clinical MRI-images (in 2 participants) was lower than the standard 1 mm³ isovoxel resolution of the in-house MRIs, the former were interpolated to 1 mm³ images. Prior to subsequent analysis steps normalizations were checked, and compared to the original images. The image analysis was performed by a neurologist experienced in clinical and experimental image analysis (HO). If lesion delineation was debatable a colleague from the Department of Neuroradiology was consulted. A lesion overlay map of the 32 patients is shown in **Figure 1B**. To assess correlations between behavior and lesion pattern the voxel-based lesion symptom software developed by Stephen Wilson was used (<https://langneurosci.mc.vanderbilt.edu/>

[resources.html](#), (Bates et al., 2003, adaptation in communication with S. Wilson)³. Based on the binary lesion maps, t-statistics determine whether a voxel correlates in a statistically significant way with performance in a behavioral measure. In other words, t-tests comparing performance between participants with versus without a lesion indicate ‘relevance’ of this voxel for the respective test.

To tackle the issue of multiple comparisons we used the permutation method (with 2,000 permutations) to correct for false positives. We report cluster-based correction, meaning that after a statistical base-map is generated, clusters surviving the threshold are corrected for multiple comparisons yielding a corrected p at the cluster level. For the first step (p of base) we used the threshold of $p < 0.001$ unless stated otherwise. Clusters are reported if they survived correction at a $p < 0.05$. Another issue is correction for volume size. For patients with large lesions, lesser performance may reflect lesser overall performance due to lesions in other regions. This can be addressed by introducing lesion size as a covariate. However, lesion size is a rough estimate of the contribution of other areas to the voxel tested and may produce false positives. Therefore, we performed all analyses with and without lesion size as a covariate. For all results reported below we explicitly state whether lesion size was included or not.

Finally, lesion-symptom approaches generally assume that performance deteriorates with a lesion while inverse correlations (i.e. ‘improvement’ in response to a lesion) are considered meaningless. In our paradigm this holds for the overall performance because more errors and longer response latencies can be expected in patients with more severe impairment. However, regarding semantic interference and associative facilitation it is conceivable that a lesion in two different brain areas may yield inverse effects. For example a lesion interfering with the retrieval of the categorical distractor would *decrease* interference while a lesion in an area

³ We checked selected results by using the software by C. Rorden allowing for non-parametric statistics (Brunner-Munzel test). This yielded largely overlapping results. <http://www.cabiatl.com/micro/npm/>; Rorden et al., 2007).

affording lexical selection should *increase* interference. Therefore correlation analyses for the interference/ facilitation effects were performed in both directions (i.e., both lower and higher values could correlate with the lesion in a specific voxel).

Data availability: Pseudonymized data are available on request.

3. Results

3.1. Group-level behavioural effects

Categorically related words should decrease whereas associatively related words should enhance naming performance compared to unrelated words. Healthy volunteers largely perform at ceiling making latency the typical outcome measure. In patients with a language-related deficit, more errors are expected, therefore we analysed both parameters independently. The results are illustrated in **Figure 2** and **Table 1**.

		LATencies [ms]			ERRors		
		mean	SD	range	mean	SD	range
ASS	rel	1417	728.6	676-3721	1.4	2.09	0-9
	unrel	1399	691.7	706-3830	1.9	2.67	0-12
	$\Delta^{\text{rel-unrel}}$	18	152.8	-174-416	-0.5	1.14	-4-1
CAT	rel	1591	685.4	747-3635	3.4	3.92	0-18
	unrel	1468	696.7	676-3750	2.4	3.88	0-16
	$\Delta^{\text{rel-unrel}}$	124	166.8	-211-502	1.0	1.77	-2-7

Table 1: Mean naming latencies (**LAT** in ms) and mean number of errors (**ERR** in whole numbers) and corresponding standard deviations (SD) and ranges. **ASS**: associatively related condition; **CAT**: categorically related condition; **rel** / **unrel**: related / unrelated prime words; $\Delta^{\text{rel-unrel}}$: difference related-unrelated conditions.

Regarding the effects of categorical and associative contexts paired, two-sided t-tests confirmed significantly longer naming latencies in the categorically related compared to the corresponding unrelated condition ($t = 4.193$, $df = 31$, $p = .0002$). No significant difference was seen for naming latencies between the associatively related and the respective unrelated condition ($t =$

0.677, $df = 31$, $p = .5033$). For error rates paired, 2-sided t-tests confirmed significantly lower error rates in the associatively related condition ($t = -2.647$, $df = 31$, $p = .013$), and higher error rates in the categorically related condition ($t = 3.298$, $df = 31$, $p = .002$) compared to the respective unrelated conditions.

On the group level, patients thus showed the effects predicted by the work in healthy volunteers (Abel et al., 2009, Henseler et al., 2014): categorical relation elicited interference, while associative relation led to facilitation. Both effects were seen for the error-rate analysis, while latencies only showed the interference effect for the categorical relation.

Due to stricter error classification and significantly lower age in the neurotypical group reported by Henseler and colleagues ($n=36$, mean age = 26.2 years ± 2.98 years, no TDCS-stimulation, i.e. ‘sham’; Henseler et al., 2014), the formal statistical comparison between the patient-cohort of the present study and the neurotypical group examined with the identical material must be considered exploratory. Mixed 2x2 ANOVAs (GROUP x RELATEDNESS) were performed. Compared to the neurotypical cohort, patients showed higher error rates in the categorical condition (main effect of GROUP, $F(1,66) = 6.442$, $p < .001$; main effect of RELATEDNESS, $F(1,66) = 10.877$, $p < .001$; no interaction, $F(1,66) = 1.720$, $p > .05$) and a trend towards higher error rates in associative contexts (trend GROUP, $F(1,66) = 3.013$, $p = .087$; main effect of RELATEDNESS, $F(1,66) = 4.555$, $p < .05$; no interaction, $F(1,66) = 2.420$, $p > .05$) despite more liberal error classification.

Patients showed higher reactions times compared to the neurotypical cohort in the associative condition (main effect of GROUP, $F(1,66) = 36.441$, $p < .001$; no effect of RELATEDNESS, $F(1,66) = 0.031$, $p = .860$; no interaction, $F(1,66) = 2.507$, $p > .05$) and in the categorical condition (main effect of GROUP, $F(1,66) = 46.505$, $p < .001$; main effect of RELATEDNESS, $F(1,66) = 30.530$, $p < .001$; significant interaction, $F(1,66) = 10.024$, $p < .05$). The item analyses confirmed the results for error rates and reaction times.

3.2. Individual variance in performance

Both parameters (LAT and ERR) greatly varied between patients, depending on severity of overall impairment and individual patholinguistic profile: LAT: $1468 \text{ ms} \pm 691.4 [701-3734]$ and ERR: $9.1 \pm 11.80 [0-55]$ (mean $\pm$ SD, [range]). Because inter-individual differences are by far larger than expected interference / facilitation effects, LAT and ERR strongly correlated across all conditions. Examples of correlations between related and respective unrelated conditions for LAT and ERR are shown in **Figure 2B**. In sum, performance in one condition is highly predictable by overall performance and/or performance in any of the other conditions.

Figure 2: (A) Comparison between categorically and associatively related conditions (CAT, blue and ASS, red bars) and their respective unrelated controls (grey bars). Categorically related words lead to longer naming latencies (LAT, left) and more errors (ERR, right). Associatively related words facilitated naming correctness (fewer errors) but did not decrease naming latency. Note that unrelated conditions (grey bars) involve different items, thus a direct comparison is not possible. * $p < .05$, ** $p < .01$, according to paired two-sided t-statistics. **(B)** Correlations between related (x-axis) and unrelated conditions (y-axis) (CAT, blue and ASS, red). In both outcome parameters (errors in whole numbers, ERR; latency in s, LAT) a strong correlation was seen indicating that the overall level of naming impairment is the major factor causing variance across the cohort. **(C)** Correlations between naming performance for categorically (CAT, y-axis) and associatively (ASS, x-axis) related items. While absolute values of ERR and LAT correlate strongly (left graphs, in absolute numbers/seconds) indicating the major influence of overall naming impairment, the difference between

related and the respective unrelated conditions shows no or non-significant correlations (right graphs). This indicates that the size of the facilitatory/ inhibitory effect of the two conditions dissociates in patients (see **Supplementary Figure SF2** for another visualisation of this dissociation between effects).

Our interest is how lesions in the language network modulate associative facilitation and semantic interference effects. Therefore, we quantified these effects by subtracting performance

in the respective unrelated from associatively and categorically related items: $\Delta\text{LAT} = \text{LAT}^{\text{related}} - \text{LAT}^{\text{unrelated}}$ and $\Delta\text{ERR} = \text{ERR}^{\text{related}} - \text{ERR}^{\text{unrelated}}$. Note that for both measures, negative (smaller) values indicate (more) facilitation while larger (positive) values indicate (more) inhibition of the naming response. **Figure 2C** demonstrates that correlations between absolute performance for CAT and ASS are abolished when the difference values are used, indicating that the size of the effect in the categorical condition *does not* predict the size of the effect in the associative condition and vice versa. The dissociation between the effects is also illustrated in **Supplementary Figure SF2**.

	lesion →	size [cm ³]	p of base	p @ cluster	max T	x	MNI y	z	aal	Harvard	BA	Dia Sph
ERR^{ALL}	↑	10.80	.001	.042	9.9	-65	-17	-25	ITG	p MTG	20	
						-51	-53	-5	ITG	t-occ MTG	37	–
LAT^{MEAN}	↑	9.46	.001	.028	5.3	-55	-44	-10	MTG	t-occ MTG	20	
						-51	-12	-18	MTG	p MTG	20	–
ΔASS^{ERR}	<i>fac</i>	4.04	.001	.036	4.9	-57	-47	-17	ITG	t-occ ITG	20	x
						-60	-20	-24	ITG	p ITG	20	
<i>cov UNR</i>	<i>inh</i>	3.67		.006	3.2	-46	14	-9	insula	t pole	?	
		0.32	.005	.032	2.9	-46	-48	9	MTG	t-occ MTG	21	–
		0.23		.040	2.8	-46	-50	13	STG	pl polare	–	
ΔCAT^{LAT}	<i>inh</i>	11.87	.010	.039	4.4	-37	11	27	IFG tri	IFG oper	–	x
						-58	19	7	IFG tri	IFG oper	44/45	
<i>cov MEAN</i>	<i>inh</i>	4.93	.005	.043	3.5	-58	19	5	IFG tri	IFG oper	–	x
						51	12	26	IFG oper	IFG oper	44	
ΔCAT^{ERR}	<i>fac</i>	0.12		.017	3.84	-45	-8	-39	ITG	a ITG	20	
		0.03	.001	.029	3.84	-68	-25	-20	ITG	p MTG	20	x
		0.01		.038	3.84	-57	-56	-10	ITG	t-occ ITG	37	
<i>cov UNR</i>	<i>fac</i>	0.08	.001	.028	3.75	-45	-8	-39	ITG	a ITG	20	x

Table 2: Significant clusters from lesion-behavior analysis. In 2nd column ↑ indicates that lesions lead to increases in overall errors / latency (ERR^{ALL} / LAT^{MEAN}); for ΔASS and ΔCAT *fac* indicates that a lesion in the cluster correlates with an increase in facilitation, while *inh* indicates an increase in inhibition. Statistical threshold at uncorrected voxel-level (*p* of base) and after multiple comparison correction at the cluster-level (*p* @ cluster) are provided. MNI coordinates of the cluster-peaks (bold) and of local peaks correspond to anatomical structures according to three standard atlases. Last column indicates whether or not lesion size was included as a covariate. **STG/ MTG/ ITG** – superior/ middle/ inferior temporal gyrus; **IFG** inferior frontal gyrus; **t pole** temporal pole; **pl polare** planum polare; **a/p/t-occ** anterior/posterior/ temporo-occipital part of the respective gyrus; **tri/oper** pars triangularis/ opercularis of IFG.

3.3. Lesion-analysis

In participants with focal brain lesions variance of both lesion-site and performance allows for statistical inference about key structures affording the respective task (Bates et al., 2003). Following this rationale we correlated different measures of overall naming performance, and the effects elicited by semantic context with individual lesion patterns. Results are described below and illustrated in **Figure 3 and 4**; details on size, anatomical site, and statistical robustness of statistically significant lesion-behaviour correlations are provided in **Table 2**.

3.3.1. Lesion patterns correlating with overall performance

Robust correlations were seen between *absolute* overall values for ERR and LAT and lesions in the MTG and ITG including the underlying white matter. **Figure 3A** shows the clusters for overall errors and mean latency across all responses (ERR^{ALL} and LAT^{MEAN}). The clusters show substantial overlap, with a somewhat more lateral extension of the cluster for ERR^{ALL}. They comprise large portions of the MTG, ITG reaching to the temporo-parietal junction. Patients with lesions in this part of the language network (details in **Table 2**) will be slower and less often correct in overall picture naming.

3.3.2. Lesion patterns correlating with facilitatory / inhibitory effects (Δ related - unrelated)

Next, we analysed the two *modulatory effects* induced by semantic context. Note that ASS is expected to facilitate naming yielding a negative Δ ERR and Δ LAT, whereas for CAT the opposite effect and therefore positive Δ ERR and Δ LAT are expected. However, lesions can interfere in a complex manner with the Δ ERR and Δ LAT: A lesion in an area considered critical for, e.g., facilitation should reduce facilitation while it is possible that lesions in another area supporting inhibition may increase facilitation. Hence, analyses for these parameters were performed in both directions. Results are illustrated in **Figure 3B**.

For the *associative* condition lower values of ΔASS^{ERR} correlated with a cluster in the MTG/ITG. This indicates a lesion in this area increases the facilitatory effect of the associatively related word prime (less errors for related when compared to unrelated words). No correlations were found for the inverse correlation, that is a decrease in facilitation for the associative condition (but see 3.3.3. for results after factoring out overall performance). For the *categorical* condition ΔCAT^{LAT} most prominently showed an inverse correlation with lesions in the IFG indicating that lesions in this area lead to an increase in naming latency for the categorical when compared to the unrelated condition. Three very small clusters in the ITG/MTG showed a positive correlation with ΔCAT^{ERR} , suggesting that lesions in these areas reduce the inhibitory effect of a categorical relation between the word and the picture.

Figure 3: Results of the lesion-behavior analysis (VLSM). **(A)** Lesions in the illustrated clusters correlate with overall higher error rates (ERR^{ALL} , pink) and higher latencies (LAT^{MEAN} , purple) in middle and inferior temporal gyrus (MTG, ITG) extending to parts of the superior temporal gyrus (STG) for latency. There is substantial overlap between both clusters. **(B)** Correlations for the difference between related minus unrelated items results in distinct clusters for either condition: ΔASS^{ERR} decreased with lesions in the inferior-middle temporal cluster (blue) indicating an increase in facilitation (less errors, blue volume). For ΔCAT^{LAT} lesions in the IFG correlated with an increase in inhibition (longer latencies, red-orange volume) while three small clusters (yellow) in the MTG/ITG and anterior ITG (a ITG) correlate with a decrease in inhibition for this condition (see **Table 2** and text for details on the clusters and **Supplemental Figure SF3** for tomographic representation of the clusters).

3.3.3. Factoring out overall performance

Because overall error rate and latency strongly determine absolute individual performance we additionally performed VLSM analyses in which overall performance was factored out by including ERR^{ALL} or LAT^{MEAN} as a covariate. As ERR^{ALL} or LAT^{MEAN} include the semantically related conditions we additionally performed the same analysis using the mean only across unrelated items. In **Table 2** the statistically relevant results are provided as *cov MEAN* and *cov UNR* respectively. These analyses confirmed the lesion-effect in the IFG cluster for ΔCAT^{LAT} (orange cluster in **Fig. 3B**) and the small temporal cluster for the inverse relation ΔCAT^{ERR} . For the associative condition, clusters in the insula, temporal pole and planum polare showed a correlation with an *increase* in ΔASS^{ERR} . This indicates that for the associative condition posterior temporal lesions increase whereas anterior temporal lesions decrease the expected facilitatory effect (see **Table 2** and **Figure 4** for a visualization).

Figure 4: Opposite effects of distinct lesion sites on associative facilitation: Lesions in the posterior temporal cluster (dark blue, identical to **Fig. 3B**) enhanced the facilitatory effect for the associative related when compared to unrelated item. When factoring out the naming performance of the unrelated condition (*covUNR*) a non overlapping anterior temporal cluster (light blue) became significant, which reduced the facilitatory effect. For details of the clusters please refer to **Table 2**.

3.3.4. Effect of lesion size

Lesion size was computed as the diameter of a sphere containing the lesion volume (DiaSph). Correlations with this measure was significant only for overall error rate ($DiaSph \leftrightarrow ERR^{ALL}$: $R^2 = 0.18$, $p = .015$). The effect of lesion size correction is controversial, therefore all analyses were performed twice, with and without lesion size as a covariate. The last column in **Table 2**

indicates whether or not lesion size was factored out in the respective analysis (DiaSph: ‘x’/‘_’). Note that all analyses reported showed at least trends ($p < 0.1$ @ the cluster level) when the corresponding other VLSM-model (with or without lesion correction) was run.

3.3.4. Comparison between subgroups with selective anterior or posterior lesions

Since previous work on a PWI-paradigm in participants with a left hemispheric lesion used group comparisons instead of the here reported VLSM approach (Piai et al., 2015, Piai and Knight, 2018) we performed an additional analysis on two subgroups of our cohort. To this end we selected participants whose lesions were restricted to either the anterior (BA44/45/46) or posterior (BA 20/21/22) hub. This yielded 8 participants in each group; lesions in the other participants affected both ($n=9$) or neither region ($n=7$). Compared to the overall mean, participants with a selective lesion in the anterior hub should show stronger inhibition in the categorical condition while this should not hold for participants with a selective lesion in the posterior hub. Conversely, a selective lesion in the posterior hub should lead to show stronger than average facilitation for the associative condition. To check this prediction we compared z-transformed latencies between the two groups (with $n=8$ in each group), predicting: $\Delta CAT^{ant} > \Delta CAT^{post}$ and $\Delta ASS^{ant} < \Delta ASS^{post}$. Results confirmed the prediction for the categorical condition (ΔCAT^{LAT} : $t=2.07$; $df=14$, $p=.029^*$; ΔCAT^{ERR} : $t=2.07$; $df=14$, $p=.061^s$) but not for the associative condition (ΔASS^{LAT} : $t=0.71$; $df=14$, $p=.756$; ΔASS^{ERR} : $t=0.357$; $df=14$, $p=.637$). Lesion distribution of the two subgroups and z-value comparisons are illustrated in **figure 5**.

Figure 5: (A) Lesion overlap of participants with lesions selectively affecting anterior (n=8) or posterior (n=8) areas. The lesions did not overlap across groups but show largest within group overlap in the two areas which resulted from our VLSM analysis (figure 3). (B) z-values for the two conditions (ASS/CAT) comparing anterior and posterior subgroups. Positive z-values indicate above average inhibition (i.e. LAT and ERR: related>unrelated). CAT shows the predicted difference between groups the inverse prediction for ASS (larger z-values for posterior group indicating above average facilitation) was not confirmed.

4. Discussion

People with aphasia (PWA) sometimes produce the word ‘cat’ when referring to a dog, albeit being fully aware of the difference between the two animals. Such errors supply clinical evidence for lesions to impair *specific* aspects of lexico-semantic competence. According to competitive models, such speech production errors are explained by activation of a lexical cohort (e.g. animals) but erroneous choice of the entry. While it is controversial at which level word production encounters competition or lateral inhibition or suffers from refractory downregulation due to repeated presentation, the fact of interference between members of a lexical cohort has been evidenced in numerous studies in neurotypical (e.g. Starreveld and La Heij, 2017, Jescheniak et al., 2014, Rose et al., 2019) and brain-lesioned participants (e.g. Ries et al., 2015, Piai and Knight, 2018, Harvey and Schnur, 2016). Evidence for the opposite effect, that is facilitation of word production by semantically related primes, has been demonstrated in neurotypical participants, with the type of relationship of the distractor (e.g. Henseler et al.,

2014) being the most robust modulator of the effect polarity (also see van Scherpenberg et al., 2020) for a discussion for a PWI paradigm including eyetracking). To capture partially contradictory results, both effects (i.e. interference and facilitation) can be conceived to co-occur, operating differentially at lexical, pre- and post-lexical levels as suggested by sensitivity to timing and the kind of semantic relation. Most parsimoniously a recent model considers the net-effect a summation of semantic context factors including the size of the cohort ('swinging-lexical-network model', Abdel Rahman and Melinger, 2009, Abdel Rahman and Melinger, 2019).

Investigating semantic context effects in patients with a lesion in the left hemispheric language network we here show a remarkably clear functional-anatomical double dissociation between net-inhibition and net-facilitation effects: lesions in the anterior hub of the network (IFG, BA 44/45) correlated with an increased interference when a categorically related word preceded the to-be-named picture. Conversely, lesions to the posterior hub (mid-posterior MTG/ITG, BA 20) increased facilitation for associatively related word primes. Notably these effects dissociate behaviourally and are not simply an effect of *overall* naming performance. The latter correlates with a large area in the STG/ MTG confirming results of previous lesion studies (Baldo et al., 2013, Pillay et al., 2017). The anatomical double-dissociation is relevant for models of word production. Moreover, while response latency are mostly reported in healthy volunteers, the effects most consistently affect *overt errors* in patients, which allows for perspectives regarding strategies for re-acquisition of lexical competence in PWA.

The findings are in line with a 'division of labour' for lexical retrieval between the two major left hemispheric language hubs: while the posterior hub affords *activation* of lexical entries including potential interference and facilitation (de Zubicaray et al., 2017, de Zubicaray et al., 2014), the inferior frontal cortex seems essential for *selection* (Belke and Stielow, 2013, Schnur et al., 2009). The relevance of selection deficits after an acquired lesion to the extended

language network has been highlighted by theoretical work (Nozari and Hepner, 2019) and has been suggested to result from a maladaptive change in the selection threshold using a drift-diffusion-model in 9 patients with left prefrontal cortex lesions (Anders et al., 2017). Hence, lesions affecting the IFG can be expected to impair selection while lesions in the posterior MTG should impact on lexical activation affecting competition or interference between cohort members. In the following we discuss the functional-anatomic dissociation of both effects and will then briefly turn to the behavioural results and a potential clinical perspective.

Lesions to left inferior frontal gyrus impair selection when lexical entries compete

We find that the size of the individual interference effect ($\Delta\text{CAT}^{\text{LAT}}$, categorically related-unrelated) correlates with lesions in the left IFG. This VLSM finding is confirmed by a subgroup analysis, in that participants with a selective lesion in the anterior hub show stronger inhibition in the categorical condition compared to participants with selective lesions in the posterior hub. Previous reports on interference effects after IFG lesion yielded partially similar but inconsistent results. In two patients with left IFG lesion, enhanced naming latencies for categorically related items was interpreted to signal IFG's central role for attentional control when resolving word-meaning interference (Vuong and Martin, 2011). Similarly 6 patients with IFG lesions showed enhanced interference in a blocked cyclic naming paradigm (Ries et al., 2015). Interestingly patients showed no difference to the healthy control group in a continuous naming paradigm. The authors therefore suggest that proactive control of selection bias is mandatory for IFG involvement. Another, elegant combined approach, investigated a blocked cyclic naming paradigm by fMRI in healthy participants and compared findings to lesion data of 12 patients (Schnur et al., 2009). Left IFG showed activation correlating with the semantic blocking interference. In conjunction with the lesion analysis a critical role of 'Broca's area' for lexical competition resolution is posited.

While these studies support a role of IFG in semantic interference, other lesion-based studies showed small (Harvey and Schnur, 2015) or no effects (Piai and Knight, 2018). In a review of over 20 neurolinguistic studies investigating semantic interference in the PWI paradigm in healthy adults and patients there was also no robust correlation between the IFG and the occurrence of semantic interference (de Zubicaray and Piai, 2019). To further complicate matters, in a study comparing 6 patients with left ventrolateral prefrontal lesions to healthy controls, patients showed enhanced phonological priming, enhanced sensitivity to any kind of lexical distractors (compared to a no-distractor condition), but showed no semantic interference effect (Piai et al., 2015). The conclusion that PFC is not relevant for interference resolution is surprising, given that healthy controls robustly showed the effect. We suggest that absence of an interference effect after PFC lesion rather points to a modulation of semantic control, interestingly abolishing rather than then augmenting the effect.

To sum up our results provide the as yet most robust evidence for left IFG lesions to enhance categorical interference in a PWI paradigm. Together with studies in healthy volunteers (e.g. Abel et al., 2012, Henseler et al., 2014) we suggest this indicates a central role of the IFG for lexical *selection* processes, especially in tasks with high competition between simultaneously activated lexical entries. This implies that the impairment in patients with frontal lesions may indeed result from a maladaptive change in the threshold at which the lexical candidate is selected (i.e. ‘criterion’ in drift-diffusion-model (DDM) terminology; Nozari and Hepner, 2019). Interestingly a recent study following the DDM rationale predicted this difference testing neurotypical and participants with pMTG and IFG lesions on a picture matching task (Todorova et al., 2020). Neurotypical participants increased the decision threshold for the more challenging related condition while drift rate did not change. Participants with lesions in the language network showed a slowed information accumulation (drift) and a lowered decision threshold, highlighting that both lexico-semantic processing and ‘conflict resolution’ contribute

to the deficit. However, for the task used in that experiment the expected difference between the MTG-lesion and the IFG-lesion group was not found.

Lesions to left posterior temporal areas increase facilitatory effect of associative primes

At first glance the second main result of our study is counterintuitive. Increased facilitation of naming when an associative prime precedes the to-be-named picture seems at odds with the notion that lesions should impair, rather than facilitate naming. However, the lesion cluster for augmented associative facilitation (blue cluster in **fig. 3B**) partially overlaps with the larger cluster in which lesions lead to more impaired *overall* naming (pink/purple clusters in **fig. 3A**). In other words, patients with overall more impaired naming will profit more strongly from associative primes, when lesioned in the smaller posterior temporal cluster. Indeed when factoring out naming performance on unrelated distractor words, a distinct lesion cluster in the anterior temporal lobe (ATL) and insular regions correlates with *lesser* facilitation for the associative prime condition (**fig. 4**, light blue cluster). The findings are consistent with a view that damage to the posterior part of MTG / ITG reduces activation of the lexical target but importantly also its competitors. In that case preserved semantic knowledge on associative relations will become more relevant, boosting the facilitatory effect. Since we did not assess non-verbal semantics, an explanation for the effect of lesions to the ATL is tentative: lesions to anterior temporal cortex may degrade the facilitatory effect of associative primes due to an impairment for supramodal semantic representation, relying on the integrity of the (bilateral) anterior temporal lobe (for an excellent review see Lambon Ralph, 2014).

We are not aware of studies showing changes in associative facilitation after focal lesions. However, partial support for the above interpretation comes from a lesion study in 15 patients with left hemispheric stroke (Harvey and Schnur, 2015). Lesions in posterior MTG enhanced interference effects for a blocked naming paradigm, in which interference is expected comparable to the categorical condition in the present study. “Noisy access to lexical

representations” is suggested to increase the interference effect. Conversely for a comprehension task (word-picture matching) lesions in anterior portions of the temporal lobe enhanced interference indicating “noisy access to semantic representations”. The partially replicated results (Piai and Knight, 2018) highlight that interference may impact at different levels of lexical retrieval (Harvey and Schnur, 2016). Regarding our findings in associative priming we suggest that if lexical and semantic representations rely on different key areas, lesions in posterior and anterior temporal lesions may well modulate associative priming in opposite directions.

Figure 6: Sketch summarizing categorical interference and associative facilitation effects in the present study. **(A)** In the intact network an associative prime ('BONE'), leads to overall facilitation since semantic facilitation is not counteracted by competition within the lexical cohort (here: pets). When a cohort member is pre-activated ('CAT') this increases interference. **(B)** Three lesion scenarios; upper left: If posterior temporal cortex (blue) is affected this leads to a noisier access to the target but also to its competitors. In this case associative facilitation is more efficient; upper right: If the IFG (red) is lesioned the selection process is impaired leading to higher error-rates and reaction time; lower left: If the anterior temporal cortex (light blue) is lesioned this reduces the supramodal semantic activation which can be considered central to associative facilitation.

More albeit indirect support for the interpretation of our results comes from two transcranial direct current stimulation (tDCS) studies. In a study using the identical paradigm and material

as the present study, anodal tDCS over left pMTG elicited a *decrease* in associative facilitation (Henseler et al., 2014). Since anodal stimulation should enhance excitability in the underlying area, the finding is perfectly complementary to our finding that *lesions* to posterior temporal cortex *increase* associative facilitation. Moreover, another study on a blocked cyclic naming paradigm showed that anodal sham-controlled tDCS over left STG *increased* the categorical interference effect (Pisoni et al., 2012). This supports the view that upregulation of the posterior temporal cortex may augment activation of the target word but likewise activation of its lexical cohort, leading to enhanced competition and interference. Therefore downregulation of the area by a lesion plausibly reduces competition within the cohort boosting the effect of associative priming.

We conclude that our data support a model in which left posterior temporal areas are pivotal to activation of the lexical target but importantly also for co-activation of lexical cohort competitors. While associative (conceptual) semantic representations may rely on anterior temporal regions as a supramodal hub, the IFG is central to selection and conflict-resolution especially in high-demand instances. Comparing patients with semantic dementia (SD) and chronic stroke patients, the causal lesion location for semantic deficits has been differentiated, despite superficially similar difficulties (Jefferies and Lambon Ralph, 2006). In line with our tentative interpretation the authors propose an amodal semantic deficit in SD patients to be housed in bilateral ATL, while in stroke patients lesions either in the IFG or posterior temporo-parietal areas yield deficits in semantic access and control.

Figure 6 provides a deliberately simplified sketch of the different scenarios. This may be the basis to detail the dynamic network architecture in future work.

Interference and facilitation are relevant for naming abilities of people with aphasia

At the group-level naming *accuracy* was reliably modulated in both semantic contexts, while *latencies* only showed the categorical inhibition but not the associative facilitation. This

highlights that the effects sometimes demonstrated as subtle latency differences in neurotypical participants, are *behaviourally relevant* in people with aphasia (PWA). Indeed errors due to categorical inhibition match clinically observable patterns for spontaneous speech of PWA, in that semantic paraphasias largely replace the target by a categorical neighbour (e.g. cat→dog) (Schwartz, 2014). Conversely, the use of facilitatory effects of associative (and supra-ordinate) relations is a key feature of the ‘semantic feature analysis therapy’ (Efstratiadou et al., 2018). We therefore believe that the highly experimental manipulation performed in the present study is potentially relevant for clinical perspectives.

Explanations for different sensitivities of the parameters to associative priming effects remain speculative, since previous studies in PWA mostly focus either on errors (Harvey and Schnur, 2015, Schwartz, 2014) or selectively report latencies (e.g. Schnur et al., 2009). A tentative explanation rests on a modelling approach comprising ‘evidence accumulation’ and ‘threshold adjustment’ as relevant but potentially selectively impaired parameters (Anders et al., 2017, Nozari and Hepner, 2019). In that vein, the ‘accumulation of evidence’ (i.e. activation of lexical candidates and cohort) is a time sensitive process. Only when this process is successful the selection challenges come into play resulting in failure (paraphasia/no response) or success. Therefore operations intrinsic to the lexicon (activation and competition) will impact on both error rate and latency, while selection depending on threshold adjustment may more prominently affect the correct/ incorrect choice of competing candidates.

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Figure and Table legends

Figure 1: (A) Picture-word paradigm. A fixation cross was followed by the distractor word in the associative condition (ASS; SOA of 300 ms, ‘Knochen’ *engl.*: bone) and the categorical condition (CAT; SOA of 100 ms, ‘Kirsche’ *engl.*: cherry). The distractor word remained on the screen during target presentation. After the voicekey was triggered the picture remained on the screen for another 3 s. Time-out for the voice key trigger was 10 s. display disappeared 3000 ms after the voice key was triggered. The time window to initiate a response was maximally 10 sec. **(B)** Lesion overlay map of the 32 patients. Coloured areas are lesioned in at least one patient. Lesion-behaviour analyses were performed in areas in which at least 3 lesions overlapped. A more detailed representation of the lesion coverage is supplied in **Supplementary Figure 1**.

Figure 2: (A) Comparison between categorically and associatively related conditions (CAT, blue and ASS, red bars) and their respective unrelated controls (grey bars). Categorically related words lead to longer naming latencies (LAT, left) and more errors (ERR, right). Associatively related words facilitated naming correctness (fewer errors) but did not decrease naming latency. Note that unrelated conditions (grey bars) involve different items, thus a direct comparison is not possible. * $p < .05$, ** $p < .01$, according to paired two-sided t-statistics. **(B)** Correlations between related (x-axis) and unrelated conditions (y-axis) (CAT, blue and ASS, red). In both outcome parameters (errors in whole numbers, ERR; latency in s, LAT) a strong correlation was seen indicating that the overall level of naming impairment is the major factor causing variance across the cohort. **(C)** Correlations between naming performance for categorically (CAT, y-axis) and associatively (ASS, x-axis) related items. While absolute values of ERR and LAT correlate strongly (left graphs, in absolute numbers/ seconds) indicating the major influence of overall naming impairment, the difference between related and the respective unrelated conditions shows no or non-significant correlations (right graphs). This indicates that the size of the facilitatory/ inhibitory effect of the two conditions dissociates in patients (see **Supplementary Figure SF2** for another visualisation of this dissociation between effects).

Figure 3: Results of the lesion-behavior analysis (VLSM). **(A)** Lesions in the illustrated clusters correlate with overall higher error rates (ERR^{ALL} , pink) and higher latencies (LAT^{MEAN} , purple) in middle and inferior temporal gyrus (MTG, ITG) extending to parts of the superior temporal gyrus (STG) for latency. There is substantial overlap between both clusters. **(B)** Correlations for the difference between related minus unrelated items results in distinct clusters for either condition: ΔASS^{ERR} decreased with lesions in the inferior-middle temporal cluster (blue) indicating an increase in facilitation (less errors, blue volume). For ΔCAT^{LAT} lesions in the IFG correlated with an increase in inhibition (longer latencies, red-orange volume) while three

small clusters (yellow) in the MTG/ITG and anterior ITG (a ITG) correlate with a decrease in inhibition for this condition (see **Table 2** and text for details on the clusters and **Supplemental Figure SF3** for tomographic representation of the clusters).

Figure 4: Opposite effects of distinct lesion sites on associative facilitation: Lesions in the posterior temporal cluster (dark blue, identical to **Fig. 3B**) *enhanced* the facilitatory effect for the associative related when compared to unrelated item. When factoring out the naming performance of the unrelated condition (covUNR) a non overlapping anterior temporal cluster (light blue) became significant, which *reduced* the facilitatory effect. For details of the clusters please refer to **Table 2**.

Figure 5: (A) Lesion overlap of participants with lesions selectively affecting anterior (n=8) or posterior (n=8) areas. The lesions did not overlap across groups but show largest within group overlap in the two areas which resulted from our VLSM analysis (figure 3). **(B)** z-values for the two conditions (ASS/CAT) comparing anterior and posterior subgroups. Positive z-values indicate above average inhibition (i.e. LAT and ERR: related>unrelated). CAT shows the predicted difference between groups the inverse prediction for ASS (larger z-values for posterior group indicating above average facilitation) was not confirmed.

Figure 6: Sketch summarizing categorical interference and associative facilitation effects in the present study. **(A)** In the intact network an associative prime ('BONE'), leads to overall facilitation since semantic facilitation is not counteracted by competition within the lexical cohort (here: pets). When a cohort member is pre-activated ('CAT') this increases interference. **(B)** Three lesion scenarios; upper left: If posterior temporal cortex (blue) is affected this leads to a noisier access to the target but also to its competitors. In this case associative facilitation is more efficient; upper right: If the IFG (red) is lesioned the selection process is impaired leading to higher error-rates and reaction time; lower left: If the anterior temporal cortex (light blue) is lesioned this reduces the supramodal semantic activation which can be considered central to associative facilitation.

Table 1: Mean naming latencies (LAT in ms) and mean number of errors (ERR in whole numbers) and corresponding standard deviations (SD) and ranges. **ASS:** associatively related condition; **CAT:** categorically related condition; **rel / unrel:** related / unrelated prime words; $\Delta^{\text{rel-unrel}}$: difference related-unrelated conditions.

Table 2: Significant clusters from lesion-behavior analysis. In 2nd column $\uparrow$ indicates that lesions lead to increases in overall errors / latency ($\text{ERR}^{\text{ALL}} / \text{LAT}^{\text{MEAN}}$); for ΔASS and ΔCAT **fac** indicates that a lesion in the cluster correlates with an increase in facilitation, while **inh** indicates an increase in inhibition. Statistical threshold at uncorrected voxel-level (**p** of base) and after multiple comparison correction at the cluster-level (**p @ cluster**) are provided. MNI

coordinates of the cluster-peaks (**bold**) and of local peaks correspond to anatomical structures according to three standard atlases. Last column indicates whether or not lesion size was included as a covariate. **STG/ MTG/ ITG** – superior/ middle/ inferior temporal gyrus; **IFG** inferior frontal gyrus; **t pole** temporal pole; **pl polare** planum polare; **a/p/t-occ** anterior/posterior/ temporo-occipital part of the respective gyrus; **tri/oper** pars triangularis/ opercularis of IFG.

Supplemental Material

Supplemental Figure SF1

Supplemental Figure SF1: Tomographic representation of lesion coverage and maximal overlap. Inset refers to Figure 1B in the main text.

Supplemental Figure SF2

Supplemental Figure SF2: Graphs illustrate that the influence of semantic for the associative effect (ΔASS) and categorical effect (ΔCAT), both representing the difference between related-unrelated items. The effect dissociate across participants. The upper graphs shows latencies (LAT). Participants are ordered according to ascending size of ΔASS (left) or ΔCAT (right). The illustrations show that the majority of the participants show the expected facilitation for ASS and interference for CAT. However, these two effects dissociate across participants. Lower graphs show the same for error rates (ERR)

Supplemental Figure SF3

Supplemental Figure SF3: The figure provides a tomographic representation of the clusters illustrated in figure 3 of the manuscript. ERR: error rate; LAT: latency; ΔASS^{ERR} : difference related-unrelated for the associative condition; ΔCAT^{LAT} : difference related-unrelated for the categorical condition.

Supplemental Table ST1:

	DiaSph	age	m.p.o.	aetiology	site	syndr.	sex
1	0.9	57	26	MCA inf	int caps	no	m
2	1.1	60	70	MCA inf	lentif	no	f
3	1.5	60	51	MCA inf	ant MCA	anomic	f
4	1.8	63	5	ICH	basal gang	residual	f
5	2.0	67	12	MCA inf	post MCA	residual	m
6	2.4	54	3	ICH/ inf	multiple	residual	f
7	2.5	58	38	mening	front	no	f
8	2.6	44	14	MCA inf	post MCA	unclassif	m
9	2.9	52	16	MCA inf	basal gang	residual	f
10	2.9	38	25	TBI	temp/par	residual	f
11	2.9	53	27	MCA inf/ TBI	ant MCA /temp	residual	m
12	3.1	46	13	MCA inf	multiple left	anomic	m
13	3.1	45	27	ICH	basal gang	residual	m
14	3.1	55	57	MCA inf	ant MCA	anomic	f
15	3.3	76	177	MCA inf	ant MCA	residual	m
16	3.8	48	12	SAH→MCA/ACA inf	ant/post MCA	residual	m
17	4.1	34	89	MCA inf	mid MCA	residual	f
18	4.1	71	189	TBI	temp/par	Broca	f
19	4.1	43	43	MCA inf	mid MCA	residual	f
20	4.2	52	5	ICH	front	residual	m
21	4.2	48	11	MCA inf	ant MCA	residual	f
22	4.3	32	41	MCA inf	post MCA	unclassif	m
23	4.3	69	14	MCA inf	ant MCA	anomic	m
24	4.5	46	25	MCA inf	post MCA	anomic	f
25	4.7	54	44	MCA inf	ant MCA	residual	f
26	4.8	44	44	astro	temp	anomic	m
27	4.8	38	31	glio	temp	residual	f
28	5.4	60	124	MCA inf	post MCA	residual	m
29	5.6	25	43	TBI	front/temp	residual	m
30	6.2	59	88	SAH→MCA inf	mid/post MCA	Broca	f
31	6.6	63	175	MCA inf	ant MCA	Broca	f
32	7.7	48	55	SAH→MCA inf	ant/post MCA	residual	m
mean	3.7	51.9	49.8				17 ♀
SD	1.57	11.7	50.6				15 ♂

Supplementary Table ST1: The table provides size (diameter of sphere corresponding to lesion volume, **DiaSph**), age and months past onset (**m.p.o.**) of the disease leading to the brain lesion. Aetiologies, aphasia syndromes (according to Aachen Aphasia Test) and rough site of the lesions are provided; abbreviations are provided below.

aetiologies: 19 ischemic infarcts (**isch**); 7 intracerebral or subarachnoid haemorrhages (**ICH/SAH**); 3 traumatic brain injuries (**TBI**); 3 tumors stable after removal: meningioma (**mening**); °II astrocytoma (**astro**); glioblastoma (**glio**)

syndromes: 18 **residual**; 6 **anomic**; 3 **Broca's**; 3 **no**; 2 **unclassifiable** aphasias (all participants had an aphasia at disease onset)

site: anterior/ middle cerebral artery territory (**ACA/MCA**); anterior, middle or posterior part of MCA territory (**ant/mid/post**); frontal, temporal or parietal lobe (**front/temp/par**); **basal ganglia**, nucleus **lentiformis**; **internal capsule**;