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BONEs not CATs attract DOGs: Semantic context effects for picture naming in the lesioned language network

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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 associatively related words (BONE → [dog]^{picture}) ease access, when compared to unrelated distractor words. 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) differ between participants. Correlating performance with lesion patterns we find support for the notion of a divergence of brain areas affording different aspects of the task: (i) lesions in the left middle temporal gyurs (MTG) deteriorate overall naming, confirming previous work; more notably, (ii) lesions comprising the inferior frontal hub (inferior frontal gyrus, IFG) of the language-network increase the interference effect for the categorical condition; on the contrary, (iii) lesions to the mid-to-posterior temporal hub (posterior middle and superior temporal gyri, pMTG/ pSTG) increase the facilitatory effect for the associative condition on error rates.

The findings can be accommodated in a neuro-linguistic framework, which localizes lexical activation but also lexical interference in posterior parts of the language network (pMTG/pITG); conversely, selection between co-activated categorically related entries is afforded by frontal language areas (IFG). While purely experimental in nature our study highlights that lesion site differentially influences specific aspects of word retrieval. Since confrontational naming is a cornerstone of aphasia rehabilitation, this may be of note when designing and evaluating novel therapeutic regimes.

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 aging (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 (cat^{context} → dog^{target}). In fact, competition within a lexical cohort is a key feature of a classical model for word production

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(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 sematic 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 ($bone^{context} \rightarrow dog^{target}$) have been shown to facilitate naming (Alario et al., 2000; 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. These temporal aspects have also been highlighted in a study investigating people with aphasia (Python et al., 2018).

The plethora of variations on the principal designs (e.g. van Scherpenberg et al., 2020, 2021), including changes in timing (e.g. Bloem et al., 2004), semantic proximity (e.g. (Rose et al., 2019) and presentation order (e.g. Wei and Schnur, 2019) has led to controversial proposals regarding the locus at which interference and facilitation of semantic relation impact on production. The net behavioral effect must be considered the summation of competing facilitatory and inhibitory effects elicited by semantic context (as elaborated in the Swinging Lexical Network Model; Abdel Rahman and Melinger, 2019). A comprehensive review of this literature is beyond the scope of the present paper. Below we briefly sketch some major aspects regarding the locus of interference.

In most models 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; Python et al., 2018). However, word-picture matching tasks, not requiring lexicalization of the competitors, have also shown semantic interference effects (Harvey and Schnur, 2016; Campanella and Shallice, 2011) suggesting a *prelexical* locus of interference in the semantic system. Based on results from continuous naming and blocked cyclic naming paradigms semantic interference has alternatively been suggested to result from incremental learning mechanisms, strengthening the connection between semantic and lexical representations (Belke and Stielow, 2013; Oppenheim et al., 2010). To complicate matters, results from some groups using the PWI task have been interpreted to show that semantic interference stems from control processes operating at *postlexical* stages of word production (Finkbeiner and Caramazza, 2006; Mahon et al., 2007). Recent models were able to reconcile prelexical and lexical accounts by distinguishing the *origin* of semantic interference on a conceptual level and the *locus* of it on the lexical level. In that view the origin of semantic contexts effects are changes in the connection strength between concepts and/or between concepts and lexical entries. The behavioral effect then manifests on a lexical level (locus) hampering lexical selection ((Roelofs, 2018); Harvey and Schnur, 2016). Indeed, interference may occur at different stages of the naming process. As an example an elegant fMRI study (de Zubicaray et al., 2012) 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).

A related 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. Moreover, an fMRI study in neurotypical participants contrasting a modified PWI paradigm and a color-naming task highlights the relevance of within versus between task requirements. The results suggest a prominent role of prefrontal areas for conflict resolution relatetd to the different tasks, while temporal areas showed higher activation for the challenges of selection within the lexical task (Spalek and Thompson-Schill, 2008). Of special relevance to the present study, these issues extend 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 may be of relevance to optimizing interventions in people with aphasia, since various confrontational naming schemes can be considered a pillar of Speech-and-Language-Therapy (SLT, e.g. Conroy et al., 2018).

To address these issues we here investigate in how far facilitation and interference can be elicited in the lesioned language network. Moreover, lesion analyses were conducted to investigate whether associative facilitation and categorical interference are dissociable processes corresponding to different '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 different aspects of 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, experimental set membership did not significantly alter involvement of the left IFG in an fMRI study using the PWI paradigm in neurotypical participants. These findings were not predicted since set membership of the distractors should increase co-activation of competitors which in turn should increase selection demands (Gauvin et al., 2020). Moreover, 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.,

[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 and La Heij 2017).

2015; Piai and Knight, 2018). Another lesion study used a variation of the PWI and a BCN paradigm to compare two groups of patients (IFG or MTG lesions, respectively) to neurotypical controls (Python et al., 2018). It pioneered the inclusion of associative contexts. Damage to the left IFG augmented semantic facilitation in associative picture-word contexts. Conversely, the MTG-lesion subgroup showed exaggerated repetition priming in blocked-cyclic-naming. The findings support models locating the threshold adjustment for lexical selection of competing candidates in the left IFG, while semantic-to-lexical connections and semantic-lexical activation are affected by damage to the left MTG.

The current study builds on this work and directly compares categorical interference and associative facilitation in a PWI paradigm in a larger group of participants with a chronic lesion in the language network. Our functional anatomic hypotheses are based on complementary evidence from neurotypical participants and lesion studies mostly using blocked cyclic and continuous naming. We predict (i) lesions in frontal areas relevant for *selection* to increase interference effects elicited by categorically related primes (Anders et al., 2017; Schnur et al., 2009; Abel et al., 2009; Badre et al., 2005), albeit negative results in some studies (Piai and Knight, 2018; Piai et al., 2015; Python et al., 2018). (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 → [dog]^{picture}), and with associative facilitation when the distractor word and the to-be-named picture share an associative semantic relation (BONE → [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±*SD*=51.9 ± *11.51* years, [range: 25–76], 16 females). The aetiologies comprised vascular but also other CNS-diseases leading to a circumscribed brain lesion.[2] 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 Aphasie 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 Material SM1*** 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 mm^3 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).

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

	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
Δ$^{rel\text{-}unrel}$	**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
Δ$^{rel\text{-}unrel}$	**124**	*166.8*	−211–502	**1.0**	*1.77*	−2–7

2.2. Stimuli

For the PWI-task participants were asked to name a target picture as fast and accurately 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 (***Fig. 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] Although selective inclusion of ischemic stroke survivors is sometimes considered the best choice for lesion-behaviour analyses, we deliberately deviate from this assumption. Ischemic strokes result from a heterogeneous underlying pathology (e.g. cardiogenic vs. generalized angiopathy) and show preferential affection of specific vascular territories. We do not claim to fully control for this bias but suggest that a broader spectrum of lesion site preference related to diverse aetiologies attenuates this problem. A second general caveat of all lesion-behavior approaches, especially with vascular pathologies, results from the fact that a large proportion of such patients show 'unspecific' white matter lesions, whose potential functional significance reduces the straightforward lesion-behavior assignment. Inclusion of younger participants with lesions resulting from e.g. the removal of a low-grade glioma or stable disease neoplasm may attenuate this general methodological limitation.

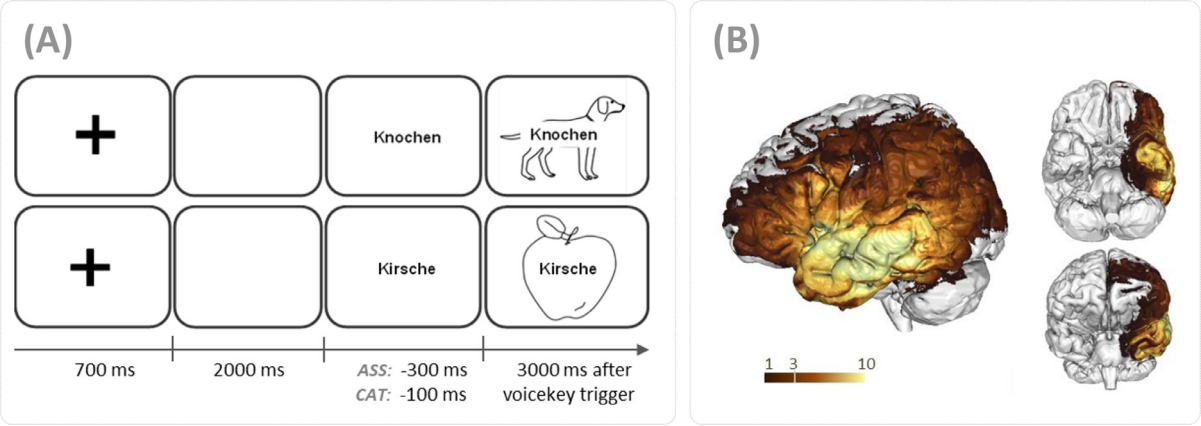

Fig. 1. (A) Picture-word Interference (PWI) paradigm. A fixation cross was followed by the distractor word in the associative condition (ASS; SOA of 300 ms, 'Knochen' *engl.*: bone) and the categorical condition (CAT; SOA of 100 ms, 'Kirsche' *engl.*: cherry). The distractor word remained on the screen during target presentation. After the voicekey was triggered the pictuire remained on the screen fpor another 3 s. Time-out for the voice key trigger was 10 s. The time window to initiate a response was maximally 10 s. **(B)** Lesion overlay map of the 32 patients. Coloured areas are lesioned in at least one patient. Lesion-behavior analyses were performed in areas in which at least 3 lesions overlapped. A more detailed representation of the lesion coverage is supplied in ***Supplemental Material SM2***.

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 served as an additional practice item and did not enter analyses; the items used were those also used during the practice block prior to the main experiment introducing the PWI paradigm. 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, only participants who showed no clinically relevant deficits in reading were included. To ensure reading comprehension for the material used in the experiment 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: each target picture was presented along with 3 words, that is the word denoting the target picture, and the related and unrelated distractor words. Participants were instructed to point to the word matching the presented picture. 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 center 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 center of the target picture (7 × 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 s. The trial structure is illustrated in ***Fig. 1A***.

The paradigm was implemented on DMDX (Version 5.134). Participants were seated in front of a TFT monitor (Samsung Sync Master 2233R2, 22 inch, 1680 × 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.

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 behavior 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 on the individual means of participants' responses for reaction times and error rates (95% confidence interval) in both semantic contexts. All analyses were performed on subject- and item-level. Statistical analyses were performed in R (3.3.2).

We additionally used a (generalized) mixed model approach to the data, based on all individual responses. Relatedness in each condition was modelled as factor of interest whereas participant and the item (i.e.

each word-picture pair) were modelled as random factors. To attenuate concerns regarding the heterogeneity of the sample we moreover included age, chronicity of the lesion, and a categorical classification of the lesion etiology as covariates. None of the covariates showed a significant effect or changed the results qualitatively when compared to the results obtained by the t-tests. The model specifications and results are provided in ***Supplemental Material SM3***.

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 and –where appropriate Spearman rank 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-behavior analysis as detailed next.

2.5. Lesion-behavior 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 mm^3 isovoxel resolution of the in-house MRIs, the former were interpolated to 1 mm^3 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 form the Department of Neuroradiology was consulted. A lesion overlay map of the 32 patients is shown in ***Fig. 1B.***

To assess correlations between behavior and lesion pattern the voxel-based lesion symptom software 'vlsm2' developed by Stephen Wilson was used (https:// langneurosci.mc.vanderbilt.edu/resources.html, Bates et al., 2003), adaptation in communication with S. Wilson). 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 2000 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. The vlsm2-software provides results based on different p-value levels of the 'base'-map (level of $p<.001$, $p<.005$ or $p<.010$ for the voxel-wise t-test before clusterwise correction). Reporting the results in ***Table 2*** the lowest respective threshold is indicated in the column 'p @ base'. Clusters are reported if they survived correction at a $p < .05$. 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. Lesion size was represented by the diameter of a sphere ('DiaS', ***Table 2***) corresponding to the volume. To account for age effects and the wide range of the chronicity of the lesion we additionally included age and month post onset ('age', 'MPO', ***Table 2***) as covariates in the vlsm2 model. We used the log-transform of months post onset, since adaptation to a lesion is more dynamic in early compared to later phases of the chronic stage. For additional details on the statistical properties of the parameters and co-variates including their intercorrelations please refer to the *Supplemental Material SM4*.

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 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 ***Fig. 2*** and ***Table 1***. For the results of an additionally performed (Generalized) Linear Mixed Model approach please refer to *Supplemental Material SM3*.

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. We additionally performed an item-based to confirm the results of the subject-based analyses: for these analyses two-sided t-tests yielded significantly longer *naming latencies* in the categorically related compared to the corresponding unrelated condition ($t = 3.287$, $df = 39$, $p = .002$) while no difference was found between the associatively related and the respective unrelated condition ($t = 1.056$, $df = 39$, $p = .298$). For *error rates* paired, two-sided t-tests confirmed lower error rates in the associatively related condition ($t = -2.380$, $df = 39$, $p = .022$), and higher error rates in the categorically related condition ($t = 2.578$, $df = 39$, $p = .014$) always 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.

The focus of the present paper is on how specific lesion sites differentially affect associative and categorical sematic context effects. An age matched control group was not included because we are not primarily interested in the effect of lesions on overall naming abilities or the overall difference between people with an acquired brain lesion and a neurotypical cohort. However, we provide the formal comparison with the group of neurotypical younger participants, who took part in the TDCS-study by Henseler et al. (2014) in ***Supplemental Material SM5***. Note that a different error classification was applied in the patient and the neurotypical cohort respectively, because the true semantic para-

Table 2
Clusters resulting 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 interference. Volume of the cluster and MNI coordinates of center of the cluster as well as the maximal T-value are provided. Following the logic of the vlsm2-approach, statistical threshold at the voxel-level (***p*** of base) is used to define clusters which are thereafter corrected for multiple comparison by permutation analysis (2000 iterations). This results in the corrected *p*-value at the cluster-level (***p*** @ cluster). Analyses were performed with and without lesion size (**DiaS**) as a covariate. In all but the last analyses months post onset (**MPO**) and **age** were entered as a covariate. The anatomical structure corresponding to the MNI of the cluster center is provided for 3 standard atlases. **MTG/ ITG** –middle/ inferior temporal gyrus; **IFG** inferior frontal gyrus; IFG^{oper} pars opercularis of IFG; **AG** angular gyrus; **t pole** temporal pole; ^{post}/ ^{sup}/ $^{t\text{-}occ}$ posterior/ superior/ temporo-occipital part of the respective gyrus;.

	lesion →	volume /cm^3	MNI x/y/z (center cluster)	max T	*p* @ base	*p* @ cluster	COV age	COV MPO	COV DiaS	aal	BA	Harvard
ERR^{ALL}	↑	11.8	−58 /−29/−12	9.93	*0.001*	*0.033*	x	x	–	MTG	20	MTG^{post}
		6.7	−57/−34/−11	8.91	*0.001*	*0.043*	x	x	x	MTG	20	MTG^{post}
LAT^{MEAN}	↑	4.8	−50/−34/−15	5.06	*0.001*	*0.039*	x	x	–	MTG	20	ITG^{post}
		9.1	−52/−28/−18	5.07	*0.005*	*0.049*	x	x	x	ITG	20	ITG^{post}
ΔASS^{ERR}	**fac**	5.9	−54/−30/−20	5.08	*0.001*	*0.032*	x	x	–	ITG	20	ITG^{post}
		6.8	−54/−30/−18	4.95	*0.001*	*0.030*	x	x	x	ITG	20	MTG^{post}
ΔCAT^{LAT}	**inh**	11.8	−45/10/13	5.06	*0.010*	*0.049*	x	x	–	IFG^{oper}	44	IFG^{oper}
		4.6	−49/14/13	4.11	*0.005*	*0.062*	x	x	x	IFG^{oper}	44	IFG^{oper}
ΔCAT^{ERR}	**fac**	0.9	−59/−54/−4	3.16	*0.005*	*0.046*	x	x	–	ITG	37	$MTG^{t\text{-}occ}$
		0.9	−59/−54/−4	4.04	*0.001*	*0.010*	x	x	x	ITG	37	$MTG^{t\text{-}occ}$
additional analysis with covariate UNRELATED words												
ΔASS^{ERR}	**inh**	6.8	−42/−49/24	3.03	*0.01*	*0.012*	*x*	*x*	–	AG	41	AG
		6.6	−46/7/−18	3.14	*0.01*	*0.015*				t $pole^{sup}$	21	t pole
		9.1	−44/6/−16	3.21	*0.01*	*0.006*	–	–	–	t $pole^{sup}$	–	t pole
		3.3	−49/−60/17	2.9	*0.01*	*0.018*				MTG	37	AG

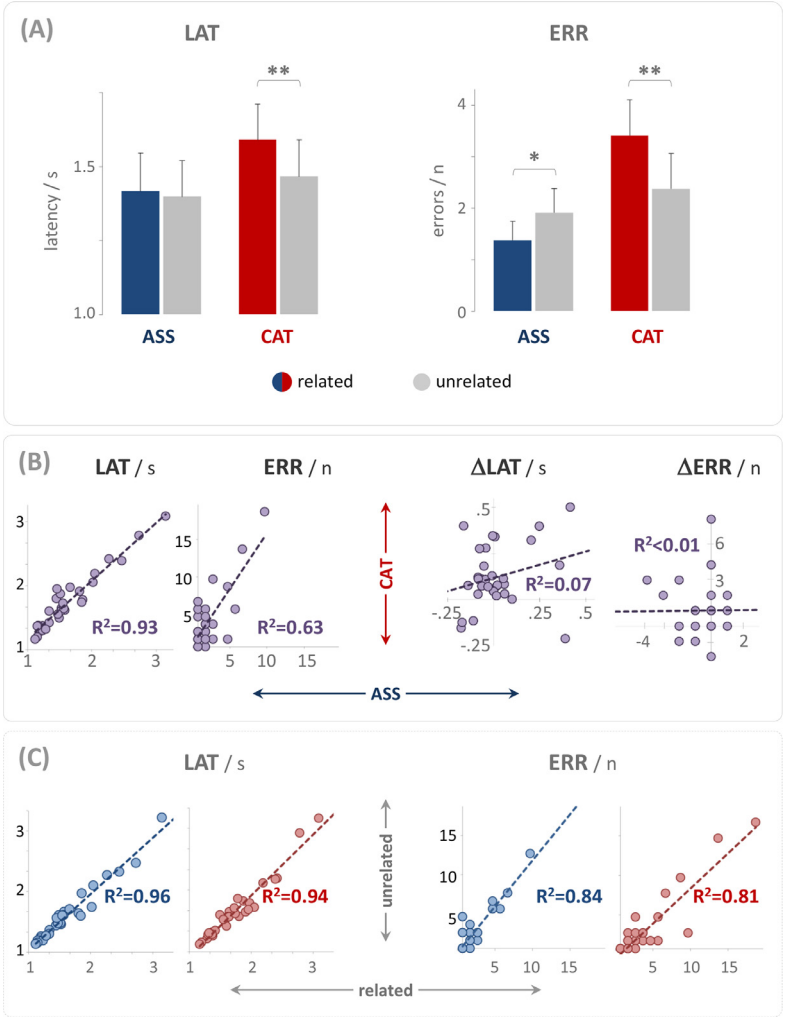

Fig. 2. (A) Comparison between categorically and associatively related conditions (CAT, blue and ASS, red bars) and their resepective unrelated controls (gray bars). Categorically related words lead to longer naming latencies (LAT, left) and more errors (ERR, right). Associatively related words facilitated naming correctness (fewer errors) but did not decrease naming latency. Note that unrelated conditions (gray bars) involve different items, thus a direct comparison is not possible. * $p < .05$, ** $p < 0.01$, according to paired two-sided t-statistics; error bars denote standard error of means (SEM) **(B)** 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 differs in patients (see ***Supplemental Material SM6*** for another visualization of this divergance of effects). Numeric details for the correlations (including Pearson's r and Spearman's r are provided in ***Supplemental Material SM4*****. (C)** Correlations between related (x-axis) and unrelated conditions (y-axis) (ASS: blue; CAT: red). Aslo for this comparison both outcome parameters (errors in whole numbers, ERR; latency in s, LAT) showed a strong correlation indicating that the overall level of naming impairment is the major factor causing variance across the cohort.

phasic errors (e.g. CAT instead of DOG) assessed in the current patient cohort with residual or mild aphasia did not occur in the neurotypical group. The comparison was therefore performed on reaction times only, and respected age as a covariate.

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 ms ±*691.4 [701–3734]* and ERR: 9.1 ± *11.80 [0–55]* (mean ±*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 ***Fig. 2C***. In sum, performance in one condition is highly predictable by overall performance and/or performance in any of the other conditions.

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: $\Delta LAT = LAT^{related} - LAT^{unrelated}$ and $\Delta ERR = ERR^{related} - ERR^{unrelated}$. Note that for both measures, smaller ('more negative') values indicate more facilitation while larger ('more positive') values indicate more interference of the naming response. ***Fig. 2B*** 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 divergence between the effects is also illustrated in ***Supplemental Material SM6;*** moreover for all depicted correlations numeric values including rank correlations are provided in ***supplemental material SM4***.

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 ***Figs. 3 and 4***; details on size, anatomical site, and statistical level of lesion-behavior correlations are provided in ***Table 2***.

3.3.1. Lesion patterns correlating with overall performance

Correlations between *absolute* overall values for ERR and LAT and lesions projected to the MTG and ITG including the underlying white matter. Correction for lesion size (DiaS in ***Table 2***) did not change the result. ***Fig. 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 ΔERR and ΔLAT, whereas for CAT the opposite effect and therefore positive ΔERR and ΔLAT are expected. However, lesions can interfere in a complex manner with the ΔERR and ΔLAT: A lesion in an area considered critical for, e.g., facilitation should reduce facilitation while it is possible that lesions in another area supporting interference may increase facilitation. Hence, analyses for these parameters were performed in both directions. Results are illustrated in ***Fig. 3B***.

For the *associative* condition lower values of ΔASS^{ERR} correlated with a cluster in the MTG/ITG. The result did not change whether or not lesion size was included as a covariate. This indicates that a lesion in this part of MTG/ITG increases the facilitatory effect of the associative condition. In other words participants with lesions comprising this region profited more form the associative prime. Surprisingly no lesion pattern was found, which leads to lesser facilitation for the associative condition. We come back to this in an additional analysis reported below (3.3.3.). For the *categorical* condition ΔCAT^{LAT} 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. When lesion size was factored out the cluster-statistics only showed a trend. A small cluster in the posterior 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 (the cluster is not visualized in ***Fig. 3B*** but is included in the visualization supplied in ***Supplemental Material SM7***).

3.3.3. Factoring out overall performance

The lesion-cluster correlating with the greater benefit from the associative primes (***Fig. 3B*** blue) overlaps with the larger cluster for overall performance (***Fig. 3A*** pink/purple). Because overall error rate and latency may distort the facilitatory or interference-effect (bottom/ ceiling effect) we additionally performed an a posteriori motivated VLSM analysis in which overall performance was factored out by including the individual mean performance on the unrelated items as a covariate (ERR^{unrel} or LAT^{unrel}). This yielded similar results for the effects in the categorical condition (data not shown), while for the associative condition a large cluster in the temporal pole and insula and a cluster around the angular gyrus showed a correlation. This suggests that lesions in these areas lead to a lesser facilitatory effect of the associative prime word. The clusters did not overlap with the overall performance correlations (pink/purple clusters Fig. 3A). The anterior cluster was larger when no covariates were entered in the vlsm2-analysis, but failed significance when lesion size was factored out. ***Table 2*** details the two clusters. ***Fig. 4*** supplies an illustration (light blue) including the above reported cluster correlating with an increase in the facilitatory effect for ASS^{ERR} (dark blue identical to ***Fig. 3B***) to ease comparison.

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 interference 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 differences in the associative and categorical context ($\Delta LAT = LAT^{related} - LAT^{unrelated}$ and $\Delta ERR = ERR^{related} - ERR^{unrelated}$) 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 of the independent one-tailed t-tests confirmed the prediction for the categorical condition (ΔCAT^{LAT}: $t = 2.07$; df=14, $p=.029^{*}$; ΔCAT^{ERR}: $t = 2.07$; df=14, $p=.061^{*}$) 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 Fig. 5.

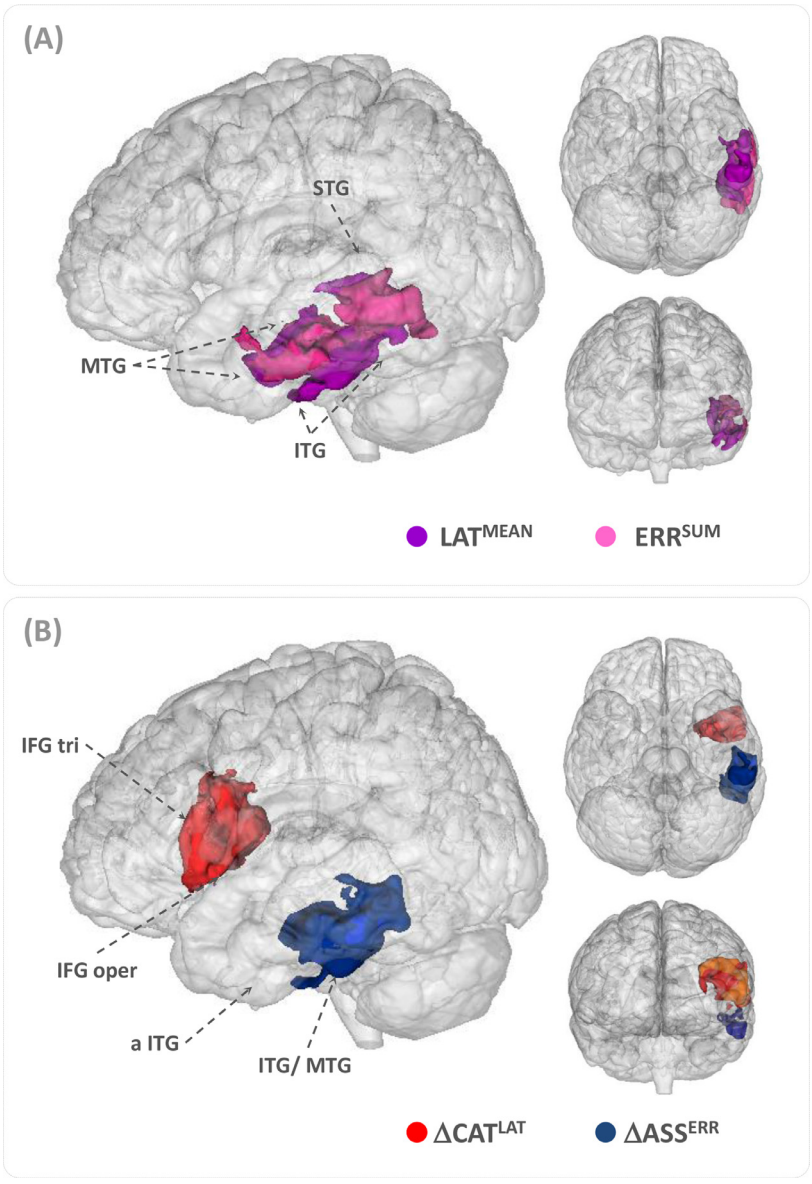

Fig. 3. Results of the lesion-behavior analysis (VLSM). **(A)** Lesions in the illustrated clusters correlate with overall higher error rates (ERR^{ALL}, pink) and higher latencies (LAT^{MEAN}, purple) in middle and inferior temporal gyrus (MTG, ITG) extending to parts of the superior temporal gyrus (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 (i.e. "more negative" value) 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 interference (longer latencies, red volume). Please see *Table 2* and text for details on the clusters and ***Supplemental Material SM7*** for a tomographic representation of the clusters including the cluster correlating with facilitation for ΔCAT^{ERR}.

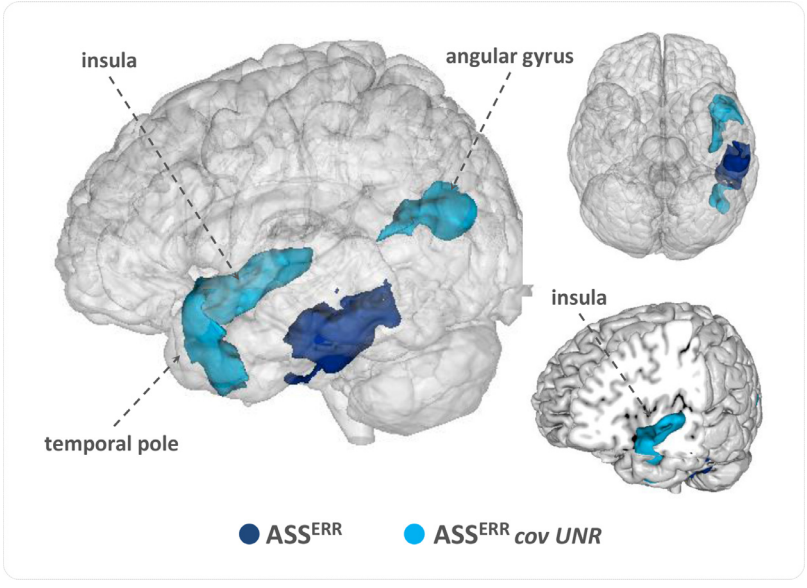

Fig. 4. Opposite effects of distinct lesion sites on associative facilitation: Lesions in the temporal cluster (dark blue, identical to *Fig. 3B*) *enhanced* the facilitatory effect for the associative related when compared to unrelated item. When factoring out the naming performance of the unrelated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

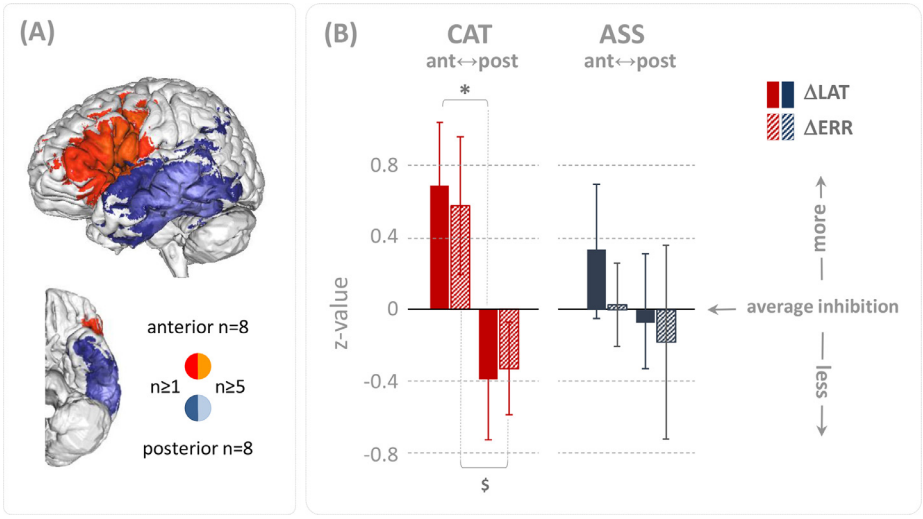

Fig. 5. **(A)** Lesion overlap of participants with lesions selectively affecting anterior (n = 8) or posterior (n = 8) areas. The lesions did not overlap across groups but show largest within group overlap in the two areas which resulted from our VLSM analysis (Fig. 3). **(B)** z-values for the two conditions (ASS/CAT) comparing anterior and posterior subgroups. Positive z-values indicate above average interference (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 and aphasic speakers, with the type of relationship of the distractor (e.g. Henseler et al., 2014; Python et al., 2018) 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 how net-interference and net-facilitation effects dissociate: 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 distinction into inferior frontal and posterior temporal areas, influencing associative facilitation and categorical interference in opposing directions 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. The present study is purely experimental and does not claim to have direct clinical implications, however understanding inhibitory and facilitatory effects of semantic context may allow to investigate their respective potential for strategies in the context of 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 concepts and their 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 via reduced connection strength between concepts and corresponding lexical entries affecting competition or interference between cohort members. In the following we discuss the different anatomical loci of both effects and will then briefly turn to the behavioural results.

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

We find that the size of the individual interference effect (ΔCAT^{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 interference 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 resoling 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 on group level (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. In addition, there is evidence for a relatively small role of the left IFG compared to left pSTG and MTG and that sufficient power is requested to detect the influence of the left IFG (Gauvin et al., 2020). The above reported results might be due to relatively small groups of aphasic speakers. 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 some evidence based on lesion mapping for left IFG lesions to affect categorical interference in a PWI paradigm. While previous group comparisons in small cohorts of aphasic speakers failed to show a significant difference between anterior and posterior lesions (Piai et al., 2015; Piai and Knight, 2018; Python et al., 2018), we confirmed the effect in a sub-sample analysis contrasting patients with isolated lesions in the anterior and posterior part of the network (n = 8 in each subgroup). Together with studies in healthy volunteers (e.g. Abel et al., 2012; Henseler et al., 2014) and in aphasic speakers in the continuous naming and blocked cyclic naming paradigm (Ries et al., 2015; Schnur et al., 2009; Harvey and Schnur, 2015) 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.

It should be mentioned that we found a small cluster projecting to the MTG/ITG in which lesions correlate with a *decrease* in errors for the categorical condition (ΔCAT^{ERR} in **Table 2**, for a visualization see **Supplemental Material SM7**). The very small size (0.9 cm^3) and the overlap with the large cluster correlating with overall naming performance (**Fig. 3A**) require caution when interpreting this result. As discussed in the next paragraph regarding the correlation with associative facilitation the overlap means that lesions in this cluster generally increase error rates across conditions, and that the very small cluster showing an inverse effect indicates a *relatively* smaller error rate for the categorical condition. Notably this cluster did not survive the additional analysis in which overall performance was factored out. We therefore refrain from highly speculative further interpretations of this finding.

4.2. 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, lesion clusters in the anterior temporal lobe (ATL) reaching to the insular cortex and angular gyrus correlate with *lesser* facilitation for the associative prime condition (***Fig. 4***, light blue cluster). The findings of this additional analysis are consistent with a view that damage to the posterior part of MTG / ITG reduces the flow of activation from the concept to the corresponding 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 increases 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.

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 concepts and their corresponding lexical entries 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 on the lexical level 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

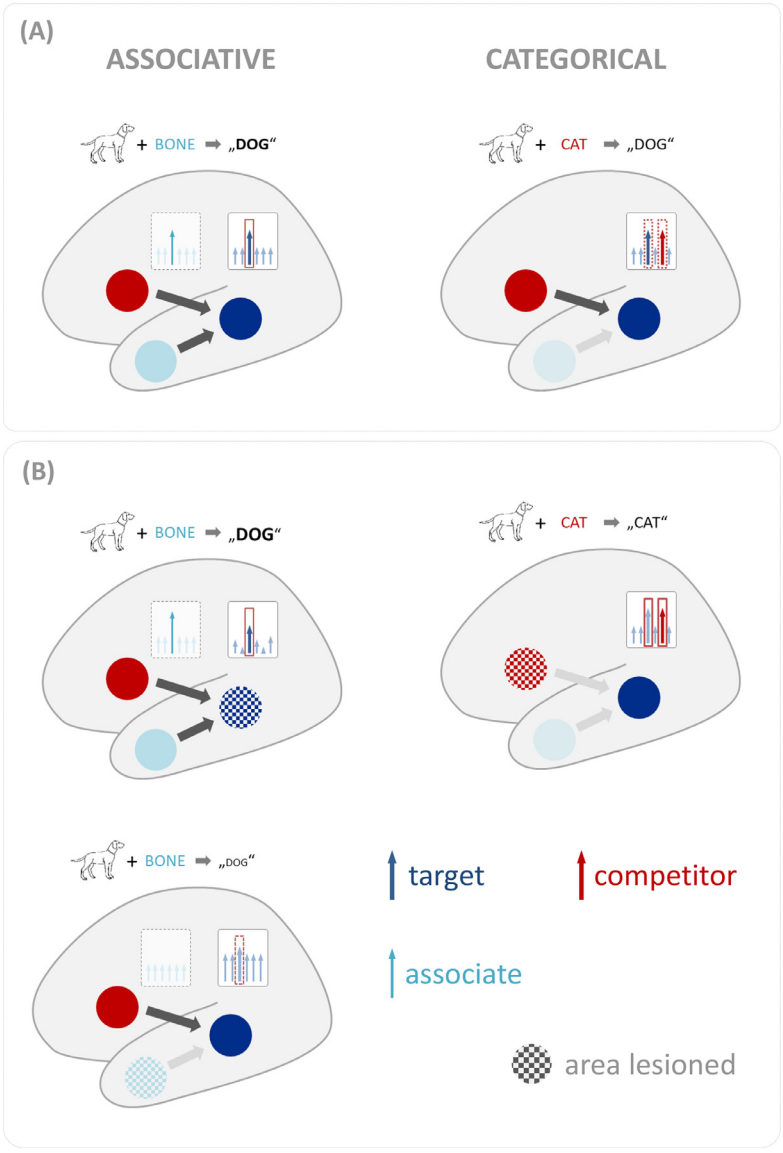

Fig. 6. Sketch summarizing categorical interference and associative facilitation effects in the present study. **(A)** In the intact network an associative prime ('BONE'), leads to overall facilitation since semantic facilitation is not counteracted by competition within the lexical cohort (here: pets). 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 noiser 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.

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.

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

4.3. 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 interference but not the associative facilitation. This highlights that the effects mostly demonstrated as subtle latency differences in neurotypical participants, are *behaviourally relevant* in people with aphasia (PWA). Indeed errors due to categorical interference match clinically observable patterns for spontaneous speech of PWA, in that semantic paraphasias largely replace the target by a categorical neighbor (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). A clear clinical perspective is certainly beyond the scope of the experimental nature of the current study. Future studies should address in how far intervention schemes for lexical-semantic training can draw on the large body of psycholinguistic results regarding confrontational naming.

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 modeling 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.

Declaration of Competing Interest

All authors declare that there is no conflict of interest.

Credit authorship contribution statement

Danièle Pino: Visualization, Methodology, Project administration, Formal analysis, Writing – review & editing. **Andreas Mädebach:** Visualization, Methodology, Formal analysis. **Jörg D. Jescheniak:** Visualization, Methodology. **Frank Regenbrecht:** Visualization, Methodology. **Hellmuth Obrig:** Visualization, Methodology, Formal analysis, Writing – review & editing.

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Supplementary materials

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