# Semantic Interference through Multiple Distractors in Picture Naming in People with Aphasia

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## Abstract

■ When we refer to an object or concept by its name, activation of semantic and categorical information is necessary to retrieve the correct lexical representation. Whereas in neurotypical individuals it is well established that semantic context can interfere with or facilitate lexical retrieval, these effects are much less studied in people with lesions to the language network and impairment at different steps of lexical-semantic processing. Here, we applied a novel picture naming paradigm, where multiple categorically related and unrelated words were presented as distractors before a to-be-named target picture. Using eye tracking, we investigated preferential fixation on the cohort members versus nonmembers. Thereby, we can judge the impact of explicit acknowledgment of the category and its effect on semantic interference. We found that, in contrast to neurotypical participants [van Scherpenberg, C., Abdel Rahman, R., & Obrig, H. A novel multiword paradigm for investigating semantic context effects in language production. *PLoS One*, *15*, e0230439, 2020], participants suffering from mild to moderate aphasia did not show a fixation preference on category members but still showed a large interference effect of ~35 msec, confirming the implicit mechanism of categorical interference. However, preferential fixation on the categorically related cohort words correlated with clinical tests regarding nonverbal semantic abilities and integrity of the anterior temporal lobe. This highlights the role of supramodal semantics for explicit recognition of a semantic category, while semantic interference is triggered if the threshold of lexical cohort activation is reached. Confirming psycholinguistic evidence, the demonstration of a large and persistent interference effect through implicit lexico-semantic activation is important to understand deficits in people with a lesion in thelanguage network, potentially relevant for individualized intervention aiming at improving naming skills. ■

## INTRODUCTION

Impaired word retrieval is a hallmark of nonfluent language production in people with aphasia (PWA). Such impairment can surface through search behavior, slower and erroneous speech (e.g., in the form of semantic paraphasias, the substitution of a target word by a semantically related word; Schwartz, 2014), or complete failure to produce certain words (anomia; Goodglass & Wingfield, 1997; Kohn & Goodglass, 1985). In psycholinguistic and neurolinguistic research, the analysis of specific deficits has shaped our understanding that word retrieval is a process consisting of several steps. In PWA, each of these steps may be selectively impaired, leading to the observed patholinguistic patterns (Levelt, Roelofs, & Meyer, 1999; Dell, Schwartz, Martin, Saffran, & Gagnon, 1997). If an object (e.g., sheep) is to be named, it is assumed that through perceptual and conceptual processes, the target is recognized and its meaning is accessed. The process includes three major steps: (i) activation of semantic features that define the item, including category membership (ANIMAL), visual (e.g., IS WHITE), or functional (e.g., PRODUCES WOOL) features (e.g., Vigliocco, Vinson, Lewis, & Garrett, 2004; Dell et al., 1997); (ii) retrieval of the object's name from the mental lexicon ("sheep"); and finally, (iii) access to the phonological representation of the target word [ʃiːp] followed by its articulatory realization.

Empirical research on both neurotypical and language-impaired populations has shown that accuracy and speed of naming vary if the respective processing levels are manipulated. For example, presenting the picture along with words phonologically or orthographically related to the target (e.g., sheep$_{\text{PICTURE}}$ and sheet$_{\text{WORD}}$) leads to facilitated and faster target naming (e.g., Abdel Rahman & Melinger, 2008; Meyer & Schriefers, 1991). This suggests phonological context to speed up the encoding of the phonological representation of the target word. In contrast, presenting context words that are semantically related to the target picture can have inhibitory effects on picture naming. In the picture–word–interference paradigm, a categorically related distractor word reduces picture naming latencies and increases error rates (e.g., Starreveld & La Heij, 1996, 2017; Wheeldon & Monsell,

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1994; Schriefers, Meyer, & Levelt, 1990; Glaser & Düngelhoff, 1984). This effect, termed "semantic interference effect," has been examined regarding the timing between distractor and target onset, the closeness of the semantic relation, and has been shown for written and auditory presentation of the distractor. Beyond the many facets of manipulation, it stands as robust evidence for the assumption that semantic context influences language production (Bürki, Elbuy, Madec, & Vasishth, 2020; de Zubicaray & Piai, 2019).

Evidence on picture–word–interference in PWA is still sparse but has great potential to shed light on the impairment of the different processing steps involved in picture naming. In an auditory picture–word interference paradigm with one anomic patient, Wilshire, Keall, Stuart, and O'Donnell (2007) report significant semantic facilitation when target and distractor are presented simultaneously (SOA = 0), whereas neurotypical participants show interference at this SOA. Notably, the anomic patient showed a trend towards semantic interference, which was only observed when the distractor was presented after the target picture onset (i.e., SOAs of +200 or +400 msec). Semantic interference effects are assumed to happen at the lexical selection stage through lexical competition, whereas priming or facilitation occurs at the conceptual level (Bloem & La Heij, 2003; Damian & Bowers, 2003; Roelofs, 1992). Therefore, the authors assume that the patient's semantic processing abilities are slowed down, prolonging the activation phase of the target's semantic representation. Thereby, at SOA = 0 msec, the distractor word would act on the pathologically prolonged semantic activation phase, not completed because of slowing. When semantic activation of the target is completed at later SOAs (+200/+400 msec), the distractor would interfere with the delayed lexical retrieval step effecting a semantic interference effect. The example demonstrates that deviations from the pattern in neurotypical participants because of lesions to the language network impair naming at specific processing steps. Indeed, a later set of studies examining picture–word–interference in participants with aphasia describe different results. Hashimoto and Thompson (2010) found significant semantic interference in RTs at SOAs = −300 and 0, with slightly bigger effect sizes but an otherwise similar pattern compared to age-matched controls. Pino, Mädebach, Jescheniak, Regenbrecht, and Obrig (2021) also report significant semantic interference for categorically related compared to unrelated distractor words in a group of 32 stroke patients (both in RTs and errors, at SOA = −100). Interference correlated with lesions to the inferior frontal cortex (IFG). Piai and Knight (2018) likewise report significant semantic interference affecting RTs and errors at SOA = 0 for a subgroup of participants with aphasia in their study. Interestingly, the subgroup largely had lesions in the left lateral-temporal cortex. Whereas the effect in RTs was similar to that of controls, this patient subgroup showed a bigger interference effect in accuracy, with significantly larger error rates for semantically related compared to unrelated distractors. According to these studies, the pattern of neurotypical participants and those with aphasia seems qualitatively comparable. Because of language production impairments in PWA, the effect shows more clearly in error rates, typically very low in neurotypical cohorts. In summary, studies in PWA support a differential impairment pattern depending on timing, semantic processing abilities, and lesion site. Although this prevents straightforward conclusions about semantic context effects in PWA, it offers a unique opportunity to study specific aspects of lexical retrieval.

In the current study, we ask how a lesion to the left-hemispheric language network alters two specific aspects of semantic context effects. To this end, we invited participants with chronic but mild aphasia after left-hemispheric circumscribed chronic brain lesion to perform a novel multiword interference paradigm previously established in neurotypical young speakers (aged 18–32 years; van Scherpenberg, Abdel Rahman, & Obrig, 2020). Naming abilities, assessed through VOT and errors, were complemented by a measure of semantic processing of the lexical cohort using eye tracking. To account for the expected large interindividual differences, we ran linear mixed models to analyze our results. Moreover, we correlated the variance of individual performance in the experiment with individual neuropsychological test scores and with individual lesion pattern.

The paradigm (introduced in van Scherpenberg et al., 2020) combines an assessment of "semantic competence" using eye tracking with a measure of lexico-semantic processing through picture naming speed and accuracy in the presence of multiple categorically related distractor words. This allows for investigating semantic and lexical processes both separately and in relation to each other. Using a circular display of eight distractor words, of which three to five belonged to one category whereas the remainder was semantically unrelated, we hypothesized that longer fixation on members of one semantic category will indicate semantic competence. This assumption rests on our finding in neurotypical, young participants using the identical paradigm. However, in people suffering from semantic dementia, it has been shown that, with increasing loss of semantic knowledge, participants spend more time fixating on unrelated foils compared to neurotypical participants with intact semantics (Faria, Race, Kim, & Hillis, 2018; Seckin et al., 2016). The task used in that study was a word-to-object matching task, also called "visual world paradigm" (Huettig, Rommers, & Meyer, 2011). Hence, impairment at the semantic processing level increases the difficulty in distinguishing between semantically related and unrelated items. In aphasia, evidence from the visual world eye tracking paradigm suggests that the participants were equally distracted from semantic competitors when having to point to the correct target picture, as were neurotypical controls (Yee, Blumstein, & Sedivy, 2008;

Experiment 1). This finding speaks for largely preserved conceptual activation of semantic relatives in typical[1] aphasia. Interestingly, phonological onset similarity disclosed differences between PWA and controls: When the distractors presented in the picture set contained competitors whose semantic relative shared the same onset as the target, neurotypical controls were more likely to fixate on a picture of an object semantically related than on an onset competitor of the target (e.g., *ham*mock$_{\text{TARGET}}$ and nail$_{\text{DISTRACTOR}}$, via *ham*mer). Whereas PWA with a Wernicke-type aphasia showed a similar semantic onset competition effect, participants with Broca's aphasia did not (Yee et al., 2008; Experiment 3). This indicates that the dynamics of lexical activation are differentially impaired in different aphasia subtypes and are reflected in fixation preference.

The combined eye tracking and picture naming paradigm used in this study allows us to investigate in how far interference in naming depends on the processing of a semantic relationship. A common explanation for the semantic interference effect through distractor words is a tradeoff between more short-lasting conceptual facilitation and longer-lasting lexical competition (Bloem, van den Boogaard, & La Heij, 2004). Although a categorically related distractor may prime the activation of the target through shared category nodes, when it comes to lexical selection, these co-activated lexical representations compete with each other, outweigh facilitation, and therefore delay retrieval (e.g., Abdel Rahman & Melinger, 2009, 2019; Melinger & Abdel Rahman, 2013; La Heij, Kuipers, & Starreveld, 2006; Wheeldon & Monsell, 1994). This competition account assumes interference is assumed to occur at the lexical selection step of the language production process.

In our paradigm, fixation on the categorically related distractor words should pre-activate the lexical cohort. Pre-activated potential lexical competitors should, in turn, hamper the selection of the lexical representation of the target picture resulting in a semantic interference effect commonly observed with single word distractors. However, if participants less efficiently distinguish between category members and nonmembers in the word set, they may not exhibit a strong semantic interference effect, because the category members did elicit strong enough activation to reach the threshold for lexical cohort activation. It follows that lexical competition and the interference effect should be smaller. In the following, we will refer to the "acknowledgment" of a semantic relationship between the distractor words, reflected by preferential fixation, as *explicit semantic processing*. Alternatively, if interference is preserved although participants show no preferential fixation of the category members, results would confirm the notion that interference is not critically dependent on the acknowledgment of the semantic cohort. This would be in line with the idea that implicit, automatic semantic activation beyond a certain threshold suffices. Evidence supporting this assumption comes from the continuous naming paradigm (Howard, Nickels, Coltheart, & Cole-Virtue, 2006), where seemingly randomly presented pictures still induce interference during naming, even when unrelated pictures are named in between. Here, cumulative interference is induced despite the absence of explicit awareness of the categorical relationship. Measuring the fixation preference while reading the words therefore provides a measure of the dynamics of semantic content processing of distractor words. Regarding the issue of implicit lexical cohort activation versus explicit acknowledgment of the respective category, we may highlight two other aspects of our paradigm: (i) Neurotypical participants did not show an effect of the number of categorically related distractor words; that is, three, four, or five related words in the distractor set elicited similarly sized interference effects. This additionally speaks for the notion that activation of lexical cohort members is largely implicit once a threshold is reached. However, in people with lesions in the lexico-semantic network, the threshold for and level of lexical cohort activation may be altered (Pino et al., 2021; Pisoni, Papagno, & Cattaneo, 2012). The current study provides information on whether lesions in specific hubs of the network modulate the automaticity of the interference effect. (ii) Participants in this and the previous studies were neither instructed to find out about the category nor was such a search of benefit for performance. The instruction was to name the ensuing target picture as fast and accurately as possible. Therefore "strategic" aspects regarding task performance are not plausible. However, the acknowledgment of categorical membership in the distractor set provides a measure of semantic competence. This is likely to act on the featural/conceptual rather than lexico-semantic level. Therefore, recognition of the category might lead to facilitation counteracting the expected interference effect. We proposed such a mechanism to explain the attenuation of the interference effect over repeated presentation, which we found in the neurotypical cohort. If explicit processing of the category is impaired because of lesions in the semantic network, we would expect to see larger and persistent interference effects in the clinical cohort examined in this study.

For the clinical group who participated in our study, high-resolution structural MRIs were available allowing for lesion site delineation. We therefore included an exploratory analysis on lesion–symptom correlations to our investigations of the behavioral effects. Importantly, this allowed us to investigate lesion–symptom correlations for eye tracking measures such as fixations to semantic foils, that is, the dynamics of semantic processing. The evidence from participants with semantic dementia points to an involvement of the left anterior temporal lobe (ATL) in semantic competence, which is the primary atrophy site in this clinical group (Gorno-Tempini et al., 2011). The ATL has been considered a semantic hub necessary to gather and retrieve conceptual information about objects (e.g., Mesulam et al., 2009, 2013; Pobric, Jefferies, & Lambon Ralph, 2007) and can therefore be hypothesized to be involved also in categorizing semantically related distractor words.

Only few studies so far have tried to relate the semantic interference effect in patients to specific lesion patterns and have yielded inconsistent results. Using voxel-based lesion–symptom mapping (VLSM), Pino et al. (2021) were able to relate the effect to lesions in the inferior frontal gyrus. More precisely, lesions in the IFG correlated with an increased semantic interference effect in naming latencies. In addition, overall latencies in the naming task were slowed down in participants with lesions in the middle temporal gyrus (MTG), suggesting an involvement of this area in the lexical selection process. This is in line with previous findings that lesions in the MTG influence picture naming in patients with aphasia (Piai & Knight, 2018). Piai and Knight report significant semantic interference in a picture–word–interference task for patients with primary lesions in the left lateral-temporal cortex (primarily in the superior temporal gyrus [STG] and MTG). On the contrary, patients with lesions in the left pFC (middle frontal gyrus and IFG) did not exhibit an interference effect. The exact role of the left pFC and IFG, in particular, during the language production process is still elusive (see also Mirman et al., 2015; Riès, Karzmark, Navarrete, Knight, & Dronkers, 2015). Recent reviews by de Zubicaray and Piai (2019) and Nozari (2020) confirm that even taking into account neuroimaging studies, there is not yet a consensus on how exactly brain regions affording language production process are involved in the semantic interference effect. Moreover, the paradigm applied here deviates in several aspects from the classical picture–word–interference paradigm. Therefore our hypotheses concerning the VLSM analysis remain tentative. As a starting point, we assume a correlation of potential effects in naming latencies with lesions in more frontal areas in the left pFC and more temporal areas in the left lateral-temporal cortex. Based on the literature regarding semantic dementia, lesions to the left ATL can be hypothesized to correlate with eye tracking patterns reflecting impairment of overall semantic competence.

# METHODS

## Participants

Thirty-two participants with chronic lesions in the left-hemispheric language network, aged 17–73 years (mean = 53, *SD* = 11.5, 10 women), participated in this study in return for monetary compensation of €9 per hour. They were selected from a database of the Clinic for Cognitive Neurology (University Hospital Leipzig) and the Max Planck Institute for Human Cognitive and Brain Sciences. Exclusion criteria for participation were additional right-hemispheric lesions, severe overall cognitive impairment, neglect or visual field deficits, severe apraxia of speech, or reading impairments. All participants had normal or corrected-to-normal vision.

All participants were diagnosed with aphasia or residual aphasia at the time of inclusion, based on the standard German assessment battery (Aachen Aphasia Test [AAT]; Huber, Poeck, Weniger, & Willmes, 1983). Of the 32 participants, 4 participants were excluded from the final sample because of too many invalid eye tracking samples resulting from technical problems with the data sampling, or errors in voice recording. In all remaining 28 participants, structural brain imaging was available allowing for lesion delineation. Twenty-three participants had a high-resolution structural MRI acquired at the Max Planck Institute for Human Cognitive and Brain Sciences; in five participants, clinically motivated MRIs with lower slice resolution were used (for details, see Lesion–Behavior Correlations section below). The overlay of all participants is shown in Figure 1. Note that, besides the temporal lobe, the IFG is covered be the lesion overlap.

Participants underwent extensive cognitive and language-related assessments. A detailed summary of each participant's demographic and clinical information as well as their cognitive and language abilities is shown in Table 1.

Experimental procedures were approved by the institutional review board of the University of Leipzig, Germany, in accordance with the Declaration of Helsinki, and written informed consent was obtained

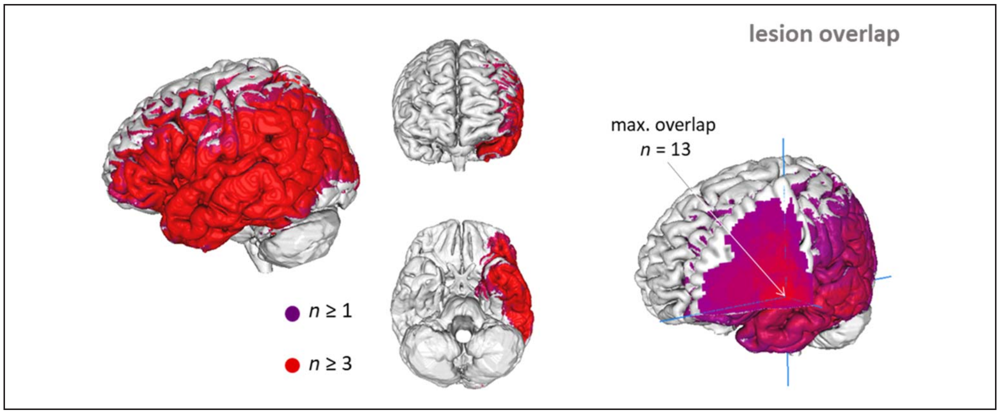

**Figure 1.** Overlay of all 28 patients in whom the analyses were performed. Note that the "field of view," which is a lesion overlap in three and more participants, covers the temporal lobe, the temporo-parietal junction, and the inferior frontal gyrus. Maximal overlap ($n$ = 13) is located in the insular region, which is seen in all studies dominated by stroke lesions.

from all participants (Ethical approval to AZ 144/18-ek, Ethics Committee University Leipzig).

## Materials

We used a variation of the picture–word interference approach, which is described in detail in van Scherpenberg et al. (2020). In this paradigm, instead of one, eight distractor words are presented simultaneously in each trial, in the shape of a circle, followed by the picture to be named. Out of these sets of eight words, a varying number (three, four, or five) belong to one semantic category, whereas the remaining words each stem from a different, unrelated category. The target pictures are either part of this semantic category or entirely unrelated to any of the distractor words. The material was constructed using seven semantic subcategories with six members each, resulting in a total of 42 items. See Table A1 (Appendix) for an overview of the stimuli.

## Apparatus

The stimuli were presented using the Psychophysics Toolbox extension (Brainard, 1997) for MATLAB (2017a, The MathWorks) on a Lenovo Thinkpad T420 laptop (14-in. monitor, 1600 × 900 pixels resolution). The words were presented in white Arial font, size 40, on a black screen, and the pictures were scaled to 5.8 × 5.8 cm (300 × 300 pixels, 5.5° of visual angle at a distance of 60 cm between the viewer's eyes and the screen). Eye movements were recorded from both eyes using a Tobii X2-60 eye tracker with a 60-Hz sampling rate. Voice responses were recorded using a Blue Yeti USB microphone.

## Design and Procedure

The variation of the number of related words in the distractor set results in a 2 × 3 design with picture TYPE (related vs. unrelated) and SIZE of lexical cohort (three, four, or five) as within-participants factors. Twelve randomized lists were created with the constraints that target pictures were separated by a minimum of two other items and that each target appeared once with a related and once with an unrelated distractor set in each block. Across each list, the participants therefore named each item 6 times. The lists were randomly assigned to the participants, by which each list was repeated a maximum of 3 times.

Each experimental session started with an instruction of the experimental procedure to which the participants consented. They were then seated in a dimly lit, soundproof room in front of the laptop and eye tracker with a distance of approximately 60 cm to the screen. A chin rest was used to minimize head movements and improve eye tracking data quality.

To familiarize the participants with the materials, each picture was presented centered on the screen with its name written underneath. In a self-paced manner, the participants named one picture after the other, and this procedure was repeated if items were not correctly named after the first familiarization (this applied only to one participant). At the start of the experimental session, the eye tracker was calibrated according to a 5-point calibration procedure, followed by three practice trials, after which any remaining questions were addressed by the experimenter.

The experimental trials were split up in three blocks with 84 trials each, in between which participants were able to take a break. Note that presentation times were increased slightly compared to the original procedure described in van Scherpenberg et al. (2020; 8 sec instead of 6 sec for the words, and 4 sec instead of 2 sec for the pictures). This accounts for additional processing costs in participants with aphasia. At the start of each trial, a fixation cross was presented in the center of the screen (0.5 sec), directly followed by the set of the eight distractor words presented in a circle around the center of the screen for 8 sec (see Figure 2 for a typical trial procedure). Participants were instructed to inspect the word set freely but were told that a minimum of three of the eight words were related to each other. During this part of the trial, participants' eye movements were recorded by a Tobii X2-60 eye tracker. Directly after the 8 sec, the distractor words disappeared, and the target picture was presented for 4 sec. Participants were instructed to name the picture as quickly and accurately as possible, and their response was recorded. After an intertrial interval of 0.5 sec, the next trial started automatically. Each trial thus lasted for 13 sec, resulting in a total experiment time of around 54 min, not including breaks.

## Lesion–Behavior Correlations

For all participants entering the analysis ($n = 28$), structural imaging was available. Twenty-three scans were performed at in-house MRI scanners (3-T Siemens MRI system Trio or Verio system, Siemens Medical Systems) including 3-D T1-weighted (1-mm$^3$ isovoxel) and Fluid Attenuated Inversion Recovery (FLAIR) images. In five participants, MRIs from clinically motivated imaging were available, with partially lower resolution (3- to 5-mm slice thickness, including FLAIR or Turbo Inversion Recovery Magnitude and T1 images). Manual lesion delineation was performed by an experienced neurologist (H. O.) primarily based on T1 images respecting the (lower resolution) FLAIR/TIRM images. This was done using MRIcron (Rorden & Brett, 2000). All images were then transformed into standard stereotactic space (Montreal Neurological Institute [MNI]) @1 mm$^3$ using SPM12 (www.fil.ion.ucl.ac.uk/spm) and the *clinical* toolbox (nitrc.org/projects/clinicaltbx/). The unified segmentation approach was applied (Ashburner & Friston, 2005), and estimation of

**Table 1.** Demographic and Clinical Information as Well as Results from Cognitive and Language Screening for All Participants ($n = 28$)

| *Part.*[a] | *Sex*[b] | *Age, years* | *m.p.o*[c] | *Syndrome* | *Etiology* | *Localization* | *Lesion size ($mm^3$)* | *AAT: Token Test (Errors)*[d] | *AAT: Naming (% Correct)*[e] | *RWT: Word Fluency Animals (Percentile)*[f] | *NVST (% Correct)*[g] | *LEMO: Synonyms (% Correct)*[h] | *LEMO: Reading (% Correct)*[i] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | W | 45 | 16 | residual | SVT | temp par | 199 | 2 | NA | NA | 0.97 | 0.90 | 0.97 |
| 2 | M | 47 | 55 | Wernicke's | Isch | watershed post | 465 | 23 | 0.88 | 1 | 0.97 | 0.85 | 0.90 |
| 3 | M | 51 | 41 | amnestic | SAH/Isch | MCA/ACA | 291 | 2 | NA | NA | 1.00 | 0.95 | 0.98 |
| 4 | M | 53 | 12 | amnestic | metastasis | precentral | 128 | 7 | NA | NA | 0.96 | 0.95 | 0.97 |
| 5 | M | 63 | 155 | residual | Isch | MCA post | 805 | 49 | NA | NA | 1.00 | 0.95 | 0.97 |
| 6 | W | 62 | 39 | residual | Isch | MCA post | 244 | 0 | NA | NA | 0.96 | 0.95 | 1.00 |
| 7 | M | 49 | 44 | residual | Isch | multiple | 104 | 3 | 0.93 | 1 | 0.92 | 0.75 | 0.95 |
| 8 | W | 60 | 29 | amnestic | ICH | temporal | 107 | 1 | 0.94 | 30 | 0.83 | 0.95 | 0.98 |
| 9 | M | 58 | 71 | Broca | ICH | basal gang/insul | 379 | 13 | 0.85 | 1 | 0.96 | 0.90 | 0.92 |
| 10 | W | 65 | 199 | Broca | Isch | MCA temp front | 1499 | 7 | 0.89 | 4 | 0.96 | 0.75 | 0.90 |
| 11 | W | 56 | 88 | residual | SAH/Isch | temporal | 283 | 0 | 0.89 | 35 | 0.97 | 0.90 | 0.97 |
| 12 | M | 48 | 62 | amnestic | ICH | basal gang/temp | 159 | 11 | 0.98 | 2 | 1.00 | 0.90 | 0.93 |
| 13 | M | 60 | 4 | amnestic | Isch | MCA front | 221 | 10 | 0.96 | 8 | 0.96 | 0.85 | 0.98 |
| 14 | M | 47 | 50 | residual | Isch | temp par | 94 | 5 | 0.97 | 82 | 0.96 | 0.95 | 0.98 |
| 15 | W | 57 | 74 | amnestic | Isch | MCA front | 536 | 11 | 0.92 | 10 | 0.92 | 0.40 | 0.63 |
| 16 | M | 56 | 7 | residual | Isch | MCA post | 260 | 12 | 0.92 | 10 | 1.00 | 1.00 | 0.85 |
| 17 | W | 27 | 72 | residual | TBI/ICH/SAH | front temp | 1138 | 4 | 0.99 | 17 | 0.96 | 0.85 | 0.95 |
| 18 | M | 41 | 62 | residual | TBI/ICH | temp/par | 128 | 2 | 1.00 | 45 | 0.96 | 1.00 | 1.00 |
| 19 | W | 51 | 46 | residual | Isch | temp insul | 385 | 0 | 1.00 | 45 | 0.96 | 0.90 | 0.85 |

**Table 1.** *(continued)*

| *Part.*[a] | *Sex*[b] | *Age, years* | *m.p.o*[c] | *Syndrome* | *Etiology* | *Localization* | *Lesion size ($mm^3$)* | *AAT: Token Test (Errors)*[d] | *AAT: Naming (% Correct)*[e] | *RWT: Word Fluency Animals (Percentile)*[f] | *NVST (% Correct)*[g] | *LEMO: Synonyms (% Correct)*[b] | *LEMO: Reading (% Correct)*[i] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | M | 51 | 93 | Broca | SAH/Isch | front temp | 2408 | 34 | 0.75 | 1 | 1.00 | 0.70 | 0.63 |
| 21 | M | 73 | 51 | residual | Isch | MCA front | 421 | 0 | 0.97 | 27 | 0.97 | 1.00 | 0.98 |
| 22 | W | 17 | 14 | amnestic | Isch | MCA large | 2638 | 0 | 0.95 | 1 | 0.88 | 0.60 | 0.82 |
| 23 | M | 49 | 8 | amnestic | HSV-encephalitis | temp. basal/mesial | 297 | NA | 0.94 | 17 | 0.96 | 0.95 | 0.98 |
| 24 | M | 56 | 65 | residual | Isch/TBI | MCA front/temp | 412 | 3 | 0.93 | 3 | 0.83 | 0.55 | 0.93 |
| 25 | M | 67 | 15 | amnestic | Isch | basal gang/thal | 233 | 0 | 0.97 | 7 | 1.00 | 0.95 | 0.93 |
| 26 | W | 62 | 126 | amnestic | SAH | temp-par | 1220 | 19 | 0.88 | 3 | 0.92 | 0.65 | 0.88 |
| 27 | M | 61 | 15 | residual | ICH | basal gang | 175 | 0 | 0.96 | 2 | 0.88 | 0.95 | 0.95 |
| 28 | M | 51 | 6 | amnestic | Isch | front temp | 376 | 0 | 0.94 | 17 | 1.00 | 1.00 | 0.97 |
| **Mean** | | **53.0** | **54.3** | | | | | | **0.9** | **16.0** | **1.0** | **0.9** | **0.9** |
| ***SD*** | | **11.5** | **46.6** | | | | | | **0.1** | **20.2** | **0.0** | **0.2** | **0.1** |

NA = not available.

[a] part = participant.

[b] W = woman; M = man.

[c] m.p.o = months post onset.

[d] AAT (Huber et al., 1983). The AAT is a German test battery for diagnosing types of aphasia after brain damage. The Token Test is used to diagnose the presence of an aphasic disorder by assessing language comprehension through pointing to and allocating geometrical shapes. A total number of errors of seven or less indicates no or residual aphasia. Eight to 11 indicate probable aphasia. Above 12 indicates aphasia. The reported values are the most recently available scores for each participant at the time of data collection.

[e] AAT Naming: The Naming subtest of the AAT assesses confrontation naming of 10 drawings of objects with simple nouns, 10 objects with compounds, 10 colors, and 10 actions. The maximum score is 120 (3 points per item). For the analyses, this was transformed into percentage correct.

[f] RWT (Aschenbrenner, Lange, & Tucha, 2001). In the RWT Word Fluency: Animals subtest, participants have to name as many animals as possible within 2 min. The scores are given as age-corrected percentiles.

[g] NVST (Hogrefe, Glindemann, Ziegler, & Goldenberg, in press). The NVST assesses nonverbal semantic abilities of categorizing objects according to situations and semantic features in several subtests. For the current study, a shortened version of three subtests was used. The subtests Gesture Production and Drawing were excluded. For subsequent analyses, a composite score was created from the percentage of correct responses across the three subtests.

[h] LEMO (Stadie, Cholewa, & De Bleser, 2013). The LEMO assesses different aspects of the language production system. In the Synonyms subtest reported here, participants have to find synonyms among four written words including one unrelated and one semantically related distractor word. The maximum score is 20. The score is given as percent correct.

[i] LEMO Reading: In the Reading subtest of the LEMO reported here, participants have to read aloud irregular and regular German words. The maximum score is 40. The score is given as percent correct.

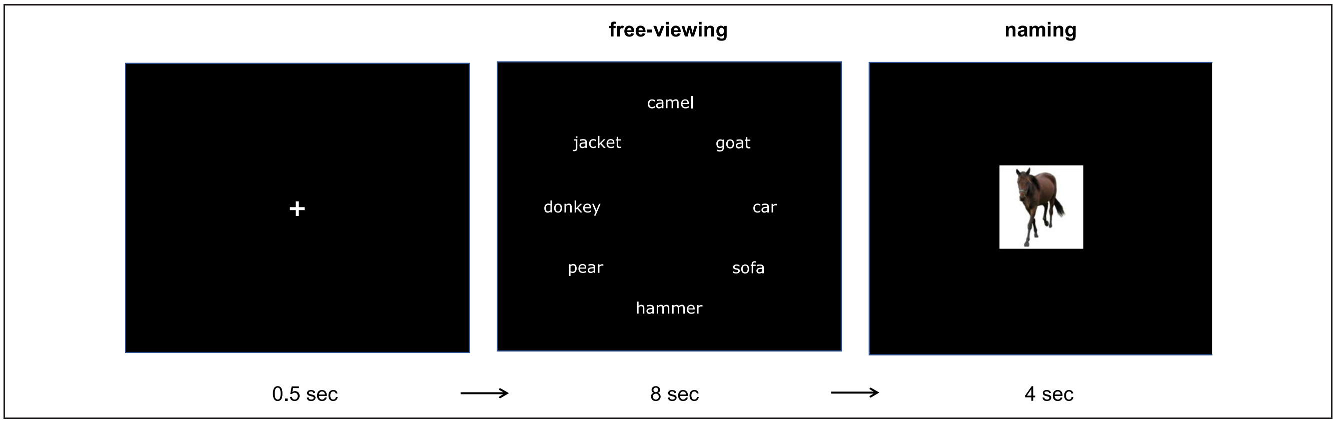

**Figure 2.** Exemplary procedure of a trial in which the word set contains a lexical cohort of three items from the semantic category "hoofed animals" (SET SIZE = 3). The target picture is part of the same semantic category (PICTURE TYPE = related). In the actual experiment, the words were presented in German.

normalization parameters was restricted to healthy tissue using predefined lesion masks (Brett, Leff, Rorden, & Ashburner, 2001).

Lesion–behavior correlations were performed along the principles of multivariate lesion–symptom mapping based on support–vector–regression (Zhang, Kimberg, Coslett, Schwartz, & Wang, 2014). The publicly available software used here is based on this approach (support vector regression lesion-symptom mapping [SVR-LSM] toolbox running in a MATLAB environment as published in the work of DeMarco and Turkeltaub [2018; https://github.com/dmirman-zz/SVR-LSM]). Multivariate approaches have the advantage that they take into account intervoxel correlations. Estimating lesion–symptom maps for all voxels simultaneously lesion mislocalization is attenuated while sensitivity to nonlinear relationships is enhanced (Zhang et al., 2014). The package used (SVR-LSM toolbox) provides several methods for controlling for lesion size. This is a central issue in all lesion–behavior approaches; most intuitively, it means that a behavioral difference between participants lesioned versus nonlesioned in a specific voxel is more likely to be because of a lesion elsewhere, if the overall lesion of a participant is larger.[2] Here, we chose lesion volume correction of both the behavioral scores and the lesion maps, as is recommended by DeMarco and Turkeltaub. Only voxels in which three and more participants showed lesions were included. The parameters analyzed were VOT as recorded by the voice key (VOT), fixation time as monitored by the eye tracker (FIX), and the performance in two of the clinical tests in percent correct: (i) nonverbal semantic assessment, Nonverbaler Semantiktest (NVST; Hogrefe et al., in press), and (ii) decision on visually presented synonyms with distractors, from the Lexikon modellorientiert (LEMO)-Battery (Stadie et al., 2013). Error rates were low and were not analyzed (in analogy to the linear mixed models regarding the behavioral analyses).

To infer statistical significance, the approach first assesses voxel-wise statistical significance by permutation testing. In this study, 2000 permutations were performed and only SVR-$\beta$-values with a $p < .005$ were regarded further. SVR-LSM considers all voxels simultaneously in a single model; however, to further reduce the multiple-comparison issue, a second step is based on FWE rate (with $p < .05$) for the cluster-extent threshold determined from the permutations (DeMarco & Turkeltaub, 2018).

## Analysis

### Picture Naming

*VOTs.* For the correct trials, voice onsets were determined at the start of each word, excluding stuttering, "uhms," or search behavior before a correct response. The VOTs were detected using the Chronset algorithm (Roux, Armstrong, & Carreiras, 2017) and checked manually using Praat (Boersma & Weenink, 2018). These were considered as the overt response, that is, the RTs.

Trials in which the voice recording was missing because of technical errors of the microphone (e.g., missing recordings or white noise) were discarded from all analyses (2.9%, $n = 198$ from all 28 participants).

Responses were considered incorrect and treated as errors when participants did not respond at all, responded falsely, or made false starts even when they consecutively produced a correct response (7.5%, $n = 510$). In total, 10.4% ($n = 708$) of all trials were classified as errors; these trials were excluded from the VOT analysis.

*Error coding.* All erroneous responses were classified according to whether they were (1) no responses, (2) semantic errors (e.g., semantic coordinates or superordinates), or (3) other errors (e.g., phonological errors, visual errors [e.g., moon → "banana"], unrelated responses).

### Eye Tracking Data

From the raw data samples, fixations and saccades were detected using the GazePath algorithm (van Renswoude et al., 2018) on the mean $x$- and $y$-coordinates of the left and right eye. Areas of interest were defined as rectangles of 270 × 170 pixels around each word in the circular word set. To correct fixations that were distorted because of head movements, we calculated the minimum euclidean distance between each data point in the fixation data frame and the eight areas of interests. This value was then used to adjust the drift of each distorted data point toward the position of the respective word in the word set.

Observations where GazePath failed to detect any fixations were excluded from the analysis ($n = 3344$, 5.9%). Combining data loss from VOT and eye tracking data, around 15% were not available for the consecutive statistical data analysis.

### *Statistical Analysis*

All statistical analyses were performed using R version 3.6.1 (R Core Team, 2016). Linear mixed effect models were run with random slopes for subjects and items, using the *lme4* package in R for linear mixed models (Version 1.1-21; Bates, Mächler, Bolker, & Walker, 2015), and $p$ values were determined using the package *lmerTest* (Kuznetsova, Brockhoff, & Christensen, 2017). All code and anonymized data can be downloaded here: osf.io/ezcgk/.

## RESULTS

### VOTs and Naming Errors

The mean VOT for the group across naming conditions is provided in Table 2 and illustrated in Figure 3. Overall, naming of semantically related pictures was 34 msec slower compared to naming of unrelated pictures, and descriptively, this interference effect was strongest for the condition with four distractor words (42 msec). On average, participants made 11 errors for related pictures and 10 errors for unrelated pictures. Given 126 trials per picture type condition, these error rates are quite low (around 8% of all trials). Considering that, across set sizes the error rates were even lower, and that, descriptively, the differences between conditions were minor, we did not analyze errors further statistically.

The effects were confirmed in a generalized linear mixed model (GLMM) with a fully specified random structure (main effects and interaction term for picture TYPE and set SIZE for both subjects and stimuli) without correlation parameters. Sliding difference contrasts were used to code the pairwise comparisons of picture type (related vs. unrelated) and set size (five vs. three and four vs. three distractor words) directly within the model.

The analysis revealed a significant main effect of picture type, indicating that related pictures were named significantly slower than unrelated pictures (estimate = 34.71, $SE = 15.08$, $t = 2.3$, $p = .021$). The main effect of set size was nonsignificant (four vs. three distractor words: estimate = −4.96, $SE = 13.61$, $t = -0.36$, $p = .715$; five vs. three distractor words: estimate = −6.16, $SE = 15.8$, $t = -0.39$, $p = .697$). Importantly, the interactions between picture type and set sizes were nonsignificant as well (for four vs. three and five vs. three distractor words both $t\text{s} < 0.54$, $p > .587$). This was confirmed by a nested model, where the effects of picture type were nested under the levels of set size. The results reveal a statistically significant interference effect at all set sizes (three distractor words: estimate = 36.25, $SE = 5.2$, $t = 6.97$, $p < .001$; four distractor words: estimate = 37.86, $SE = 7.28$, $t = 5.2$, $p < .001$; five distractor words: estimate = 28.88, $SE = 6.54$, $t = 4.42$, $p < .001$). This means that, contrary to our predictions, additional distractor words did not significantly affect naming latencies. These results are summarized in Figure 3. For comparison, we provide results by neurotypical participants ($n = 24$) described in van Scherpenberg et al. (2020) in the same plot.

When comparing the current clinical cohort to the previously reported neurotypical cohort of young participants, age and age range differ dramatically. To address an age group effect formally, we are currently investigating younger (18–32 years) and older (60–70 years) participants with the paradigm (paper in preparation). To assess the additional aspect of age range, we performed the current and following analyses including age as a covariate in the GLMM. This yielded the qualitatively same results (see Appendix Table B1).

Establishing this novel paradigm in young, neurotypical participants, we found an item repetition effect.

**Table 2.** Mean VOTs in Milliseconds and *SEM*s for Each Naming Condition

| *Distractor Set Size* | *3* | | *4* | | *5* | | *Total* | |
|---|---|---|---|---|---|---|---|---|
| Picture type | related | unrelated | related | unrelated | related | unrelated | related | unrelated |
| Mean VOTs in ms | 1333.08 | 1302.23 | 1335.94 | 1293.94 | 1326.52 | 1297.11 | 1331.86 | 1297.75 |
| SE | 16.07 | 15.25 | 15.65 | 14.78 | 16.19 | 15.24 | 11.90 | 11.25 |
| Interference | 30.85 | | 42.00 | | 29.41 | | 34.11 | |
| Mean no. of errors | 4.74 | 5.06 | 3.86 | 3.86 | 4.40 | 4.05 | 10.96 | 10.32 |

Values are adjusted for within-participant designs following Morey (2008).

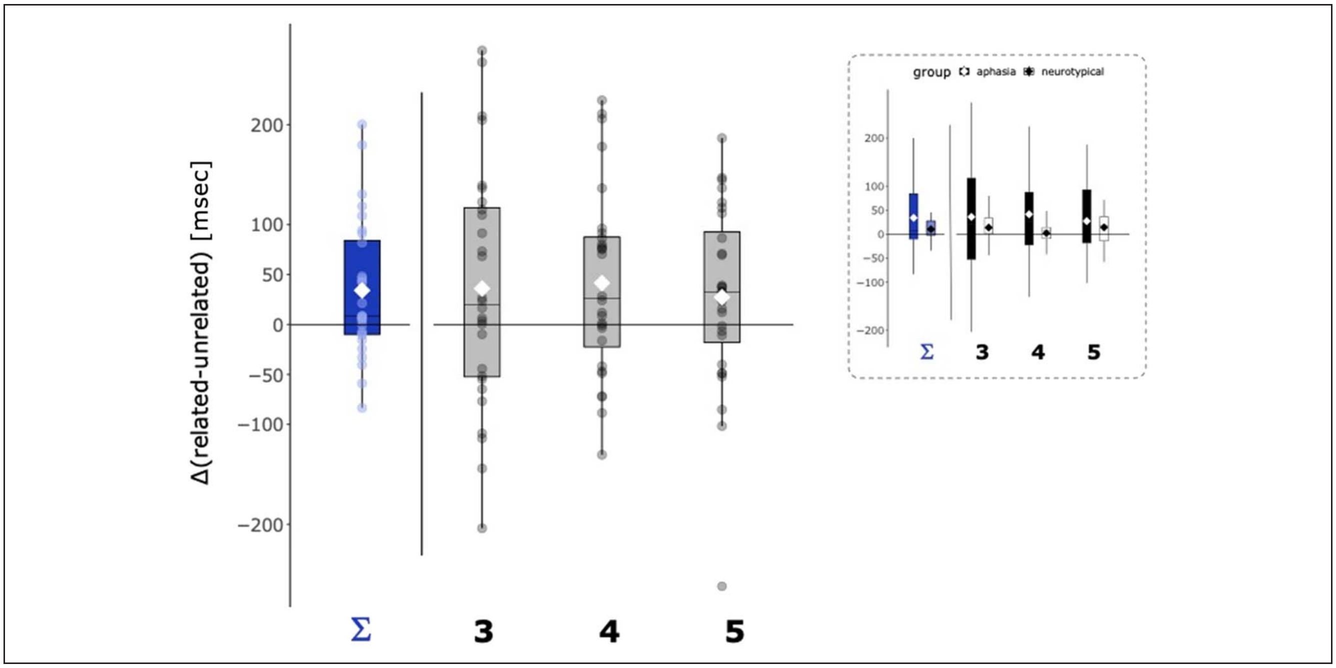

**Figure 3.** Interference effect in total and across number of distractor words for participants with aphasia. Boxplots show mean, median, upper and lower quartiles, and range. Dots represent individual means. For numerical values, see Table 2. The inset shows a comparison of the effect between the participants with aphasia (darker shades) and neurotypical participants (lighter shades, $n$ = 24; see van Scherpenberg et al., 2020, for details).

Item repetition had an effect on naming latencies and the semantic interference effect, reducing both significantly across repetitions. We therefore ran another model for the clinical population in the current study, including repetition as a covariate (mean-centered and standardized) in interaction with picture type. The fully specified random structure was supported and reached convergence. This analysis revealed main effects of picture type (estimate = 39.75, $SE$ = 15.19, $t$ = 2.62, $p$ = .009) and repetition (estimate = −65.68, $SE$ = 9.94, $t$ = −6.61, $p$ < .001). In contrast to the neurotypical population, however, results in the clinical population show no interaction between picture repetition and picture type (estimate = 8.02, $SE$ = 15.17, $t$ = 0.53, $p$ = .597). This indicates that, although naming latencies decreased linearly by ~66 msec, on average, across repetitions, the semantic interference effect remained stable in the clinical population as illustrated in Figure 4, again including the comparson to the neurotypical population. The results remained the same when including age as a covariate in the model (Appendix Table B2).

## Fixation Durations

Prior to the naming task, participants viewed the distractor words arranged in a circle and fixations on these words were analyzed separately. Note that, in each trial, three, four, or five words were members of a semantic category whereas the remaining (five, four, or three, respectively) were nonmembers. To evaluate statistically the difference in fixation durations between the category members versus nonmembers, we ran a generalized linear mixed model with fixation durations as the dependent variable and word type (member vs. nonmember) and set size (three, four, or five) as fixed effects. All fixed effects were coded with sliding difference contrasts. Again, we accounted for by-subject and by-stimulus random slopes, and the final converging model included a fully specified random structure, without correlation parameters and one contrast of the factor set size. None of the contrasts were significant, indicating no significant difference between fixation durations on category members versus nonmembers, independent of the number of categorically related words (all $t$s < 0.874, all $p$s > .382; see Figure 5 and Figure C1 [Appendix] for details). As described in the work of van Scherpenberg et al. (2020) and illustrated in Figure 5, this finding is clearly different from the pattern we observed with neurotypical participants, who fixated longer on category members independent of set size. Including age as a covariate, we observe that this main difference in fixation duration remains nonsignificant (see Appendix Table C1).

Subsequently, we investigated whether fixation durations on category members had an effect on naming latencies, in interaction with picture type. We therefore added fixation durations as a covariate (mean-centered and scaled) to a generalized linear mixed model, with VOT as dependent variable and picture type as fixed effect. The model with a fully specified random structure without correlation parameters converged.

The analysis revealed no influence of fixation durations on naming latencies (estimate = 2.88, $SE$ = 10.33, $t$ = 0.28, $p$ = .781) and no interaction with picture type (estimate = 10.04, $SE$ = 15.81, $t$ = 0.64, $p$ = .525). The main

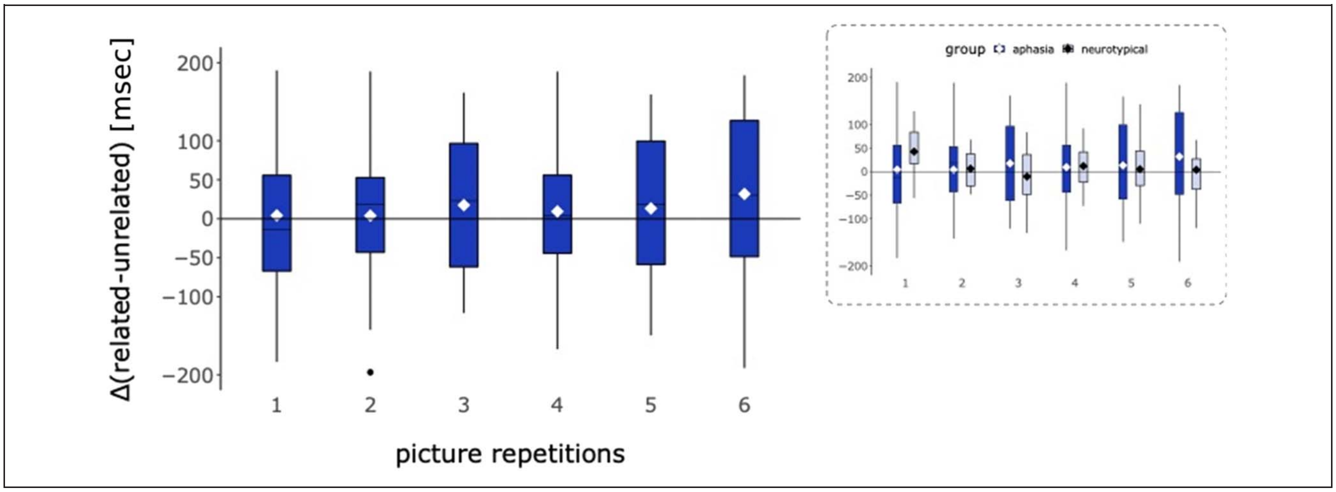

**Figure 4.** Interference effect across picture repetitions for participants with aphasia. Boxplots show mean, median, upper and lower quartiles, and range. The inset shows a comparison of the effect between the participants with aphasia (darker shades) and neurotypical participants (lighter shades, $n = 24$; see van Scherpenberg et al., 2020, for details).

effect of picture type remained significant (estimate = 31.27, *SE* = 15.47, $t = 2.02$, $p = .043$).

## Correlations with Clinical Linguistic Measures

Finally, we correlated a selection of the clinical linguistic measures with our experimental effects. The linguistic measures (see Table 1) included reading abilities (LEMO Reading), synonym judgments (LEMO Synonyms), general naming abilities (AAT Naming), semantic word fluency (Regensburger Wortflüssigkeits-Test [RWT]: Animals), and nonverbal semantic abilities (NVST). We were particularly interested in how these measures might be related to the semantic interference effect, or the difference in fixation durations between category members and nonmembers. These individual effect sizes were taken from the estimated Subject coefficients of the linear mixed models described above to account for interindividual or item-based variation. The semantic interference effect did not correlate with any of the test scores. However, performance in the NVST correlated with the differences in fixation durations to category members versus

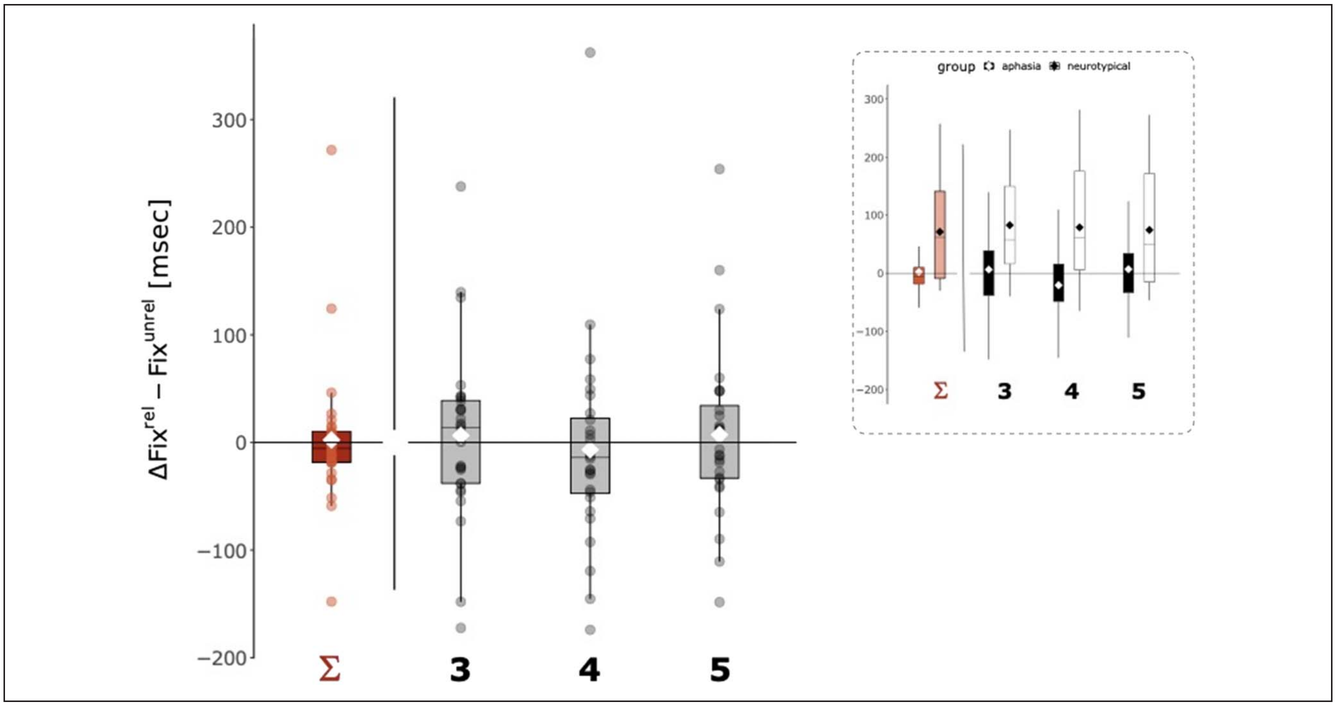

**Figure 5.** Fixation durations for each word as part of the distractor word set for participants with aphasia. Boxplots show mean, median, upper and lower quartiles, and range. Dots represent individual means. The inset shows a comparison of the effect between the participants with aphasia (darker shades) and neurotypical participants (lighter shades, $n = 24$; see van Scherpenberg et al., 2020, for details).

nonmembers (rho = .463, $p$ = .013): The better participants scored in the NVST, the more they preferentially fixated on categorically related words, indicating acknowledgment of the semantic category. The (Spearman rank) correlations are summarized in Table D1 (Appendix).

## Lesion–Behavior Correlations

In our exploratory lesion–behavior analysis, we used mean individual VOTs and fixation times (FIX) during the exploration of the eight distractor words. For both parameters, we analyzed the respective value for the related and the unrelated conditions and their difference. Moreover, we correlated individual lesions with individual scores in the clinical tests.

For VOT, the behavioral score was the mean response time after picture onset with VOT$^{\mathbf{rel}}$ if the picture belonged to the same category as the semantic category in the distractor word set, and VOT$^{\mathbf{unr}}$ for pictures unrelated to the category. For the analyses, the respective other parameter was entered as a covariate in the SVR-LSM model (i.e., VOT$^{\mathbf{rel}}$ as a covariate for the analysis of VOT$^{\mathbf{unr}}$ and vice versa). An additional analysis was performed with the mean difference between related and unrelated conditions ($\Delta$(VOT$^{\mathbf{rel}}$ − VOT$^{\mathbf{unr}}$)). In this case, VOT$^{\mathbf{mean}}$ was introduced as a covariate in the SVR-LSM. For fixation time, the same values were calculated (i.e., FIX$^{\mathbf{rel}}$, FIX$^{\mathbf{unr}}$, and $\Delta$(FIX$^{\mathbf{rel}}$-FIX$^{\mathbf{unr}}$)). Regarding the interpretation of the results, it is relevant to consider the assumptions of the SVR-LSM model. Although for overall VOT it is intuitive that larger values are expected as a sequel of a lesion in a relevant brain area, the strength of interference effect may result in a seemingly paradoxical behavior. That means that a lesion may attenuate the interference effect, thereby resulting in relatively shorter VOT compared to a participant without a lesion. Therefore, results listed in Table 3 and illustrated in Figure 6 and Figure 7 regard lesion sites that correlate with a deviation from the expected behavior (which has been documented in the neurotypical young control group). The clusters listed and illustrated did not survive the more conservative cluster-based correction for multiple comparisons. Therefore, results must be interpreted with caution.

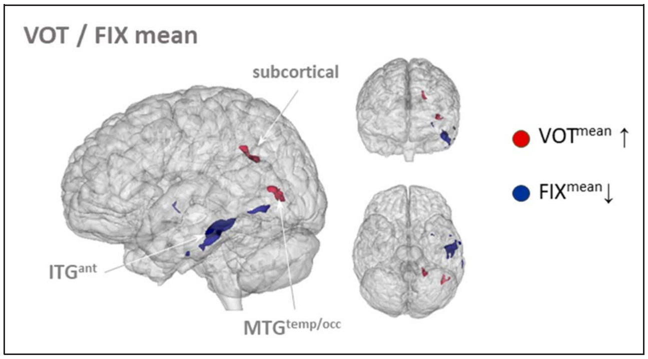

**Figure 6.** Clusters (uncorrected) corresponding to shorter fixation during the presentation of the distractor words (FIX$^{\mathbf{mean}}$↓, blue) and longer naming latencies (VOT$^{\mathbf{mean}}$↑, red). Specifications of the clusters are provided in Table 3.

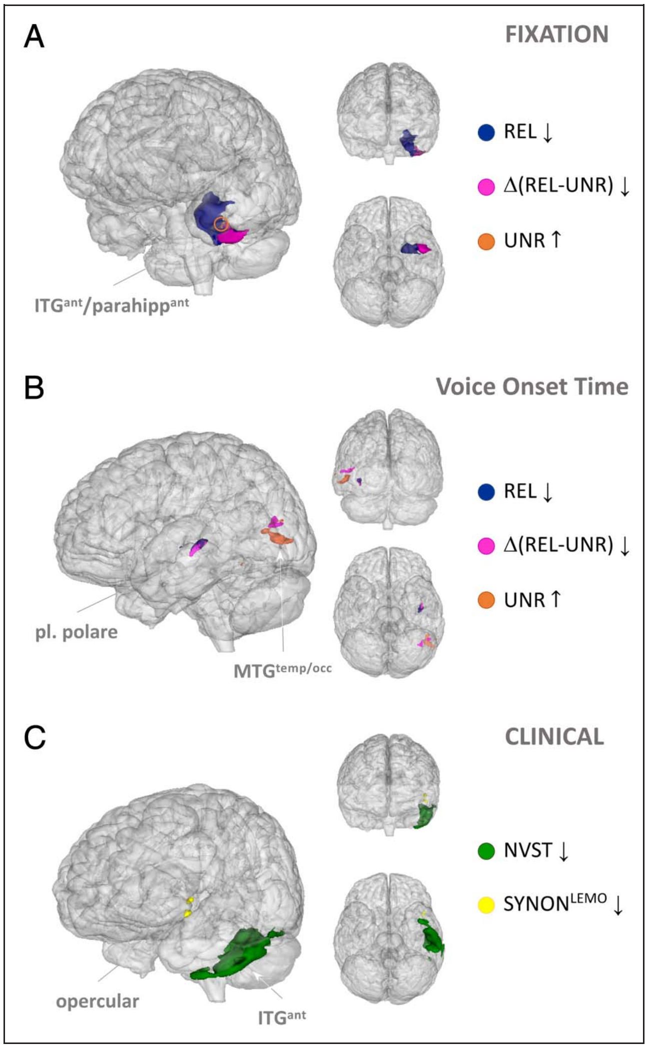

**Figure 7.** Clusters (uncorrected) corresponding to the behavioral effects of VOT (VOT$^{\mathbf{rel}}$, VOT$^{\mathbf{unr}}$, $\Delta$VOT$^{\mathbf{rel\text{-}unrel}}$) and FIX (FIX$^{\mathbf{rel}}$, FIX$^{\mathbf{unr}}$, $\Delta$FIX$^{\mathbf{rel\text{-}unr}}$) as well as the clinical measures assessing semantic abilities (NVST and SYNON$^{\text{LEMO}}$). Specifications of the clusters are provided in Table 3.

As illustrated in Figure 6, lesions in a cluster in the anterior inferior temporal gyrus (ITG) reduced mean fixation time during the presentation of the distractor words, whereas a cluster in the posterior portion of the MTG increased VOT signaling slower naming. The second cluster corresponding to VOT increases is located in the subcortical white matter.

Regarding the question in how far lesions in specific areas may modulate the categorical analysis during the presentation of distractor words (FIX), Figure 7A illustrates that lesions in a large cluster in the ATL correspond to a decrease in relative fixation of the related words. This

**Table 3.** Results of the SVR-LSM

| | | | | *MNI of Peak* | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | *Size mm$^3$* | *Dia mm* | *$p^{max}$* | *x* | *y* | *z* | *Harvard* | *aal* | *Brod* |
| *VOT* | | | | | | | | | |
| mean ↑ | 273 | 4.0 | *.001* | −45 | −55 | 0 | MTG$^{\text{temp-occ}}$ | MTG | 37 |
| | 243 | 3.9 | *.002* | −27 | −51 | 26 | *n.d.* | *n.d.* | *n.d.* |
| Δ (rel-unr)↓ | 218 | 3.7 | *.001* | −47 | −55 | 3 | MTG$^{\text{temp-occ}}$ | MTG | 37 |
| | 133 | 3.2 | *.001* | −41 | −6 | −12 | pl. polare | STG | *n.d.* |
| rel ↓ | 222 | 3.8 | < *.001* | −41 | −6 | −12 | pl. polare | STG | *n.d.* |
| unr ↑ | 407 | 4.6 | *.002* | −47 | −54 | −1 | MTG$^{\text{temp-occ}}$ | MTG | 37 |
| *FIX* | | | | | | | | | |
| mean↓ | 957 | 6.1 | *.001* | −48 | 1 | −41 | ITG$^{\text{ant}}$ | ITG | 20 |
| | 301 | 4.2 | *.001* | −67 | −40 | −20 | ITG$^{\text{ant}}$ | ITG | 20 |
| Δ(rel-unr)↓ | 620 | 5.3 | *.001* | −43 | −1 | −43 | ITG$^{\text{ant}}$ | ITG | 20 |
| rel ↓ | 2316 | 8.2 | *.002* | −34 | 3 | −42 | temp pole | temp pole$^{\text{mid}}$ | 36 |
| unr ↑ | 81 | 2.7 | *.004* | −34 | 3 | −42 | temp pole | temp pole$^{\text{mid}}$ | 36 |
| *CLINICAL* | | | | | | | | | |
| NVST % ↓ | 4643 | 10.3 | < *.001* | −46 | −9 | −46 | ITG$^{\text{ant}}$ | ITG | 20 |
| SYN % ↓ | 103 | 2.9 | < *.001* | −48 | 17 | −13 | temp pole | temp pole$^{\text{sup}}$ | 38 |

The largest clusters for the respective parameters are listed. Note that, in the clusters, each voxel passed the $p < .005$ threshold, whereas none of the clusters survived more conservative cluster-based correction. The table provides the cluster size in mm$^3$ and as the diameter of a sphere corresponding to the volume (Dia). $p^{\max}$ denotes the maximal statistical threshold reached in the cluster. MNI coordinates and regions according to three different atlases are provided (Harvard-Oxford atlas, Automated anatomical labeling atlas, Brodman atlas; n.d. indicates not defined in the atlas). The direction of the arrow in the first column indicates the direction in which a lesion would modulate the parameter, that is, ↓: lesion will decrease the numerical value and ↑: lesion will increase the numerical value.

cluster is closely collocated to a cluster in which lesions correspond to a decrease in the difference between relative fixation of related minus fixation of the unrelated distractor words ($\Delta$FIX$^{\textbf{rel-unrel}}$↓). A much smaller cluster in which lesions correspond to increasing relative fixation on unrelated words (FIX$^{\textbf{unrel}}$↑) largely overlaps with parts of the two above clusters. The fact that lesser fixation on related words (FIX$^{\textbf{rel}}$↓) is the more prominent cluster confirms the intuitive prediction that difficulties to recognize the categorical relationship should mostly decrease preferential fixation of related words. This finding is complemented by a correlation of a large cluster in the ATL (anterior part of the ITG) with a decrease in the performance in the NVST test, assessing nonverbal semantic abilities (Figure 7C).

Regarding the interference effect on naming, the results suggest that lesions in a cluster of the posterior MTG and another cluster in the STG/planum polare correlate to smaller interference ($\Delta$VOT$^{\textbf{rel-unrel}}$↓; Figure 7B). While the posterior cluster (MTG) is close to a cluster in which VOT for unrelated pictures increases (VOT$^{\textbf{unrel}}$↑), the cluster in the mid STG partially overlaps with a decrease in VOT for related items (VOT$^{\textbf{rel}}$↓).

## DISCUSSION

Lesions to the left-hemispheric language network regularly interfere with the ability of prompt and correct retrieval of words. Clinically, this results in the slowing of speech production and erroneous choice of lexical entries. One common type of such errors is semantic paraphasias leading to the substitution of a target word by a semantically related word (Schwartz, 2014). Although it is the clinical goal of speech and language therapy to restore fast and precise lexical retrieval in PWA, error patterns in these speakers may shed light on how our brain supports the remarkable ability of seemingly effortless language production. This, in turn, may allow for developing theoretically grounded therapy schemes also for confrontational naming training, a cornerstone of speech and language therapy in aphasia (Off, Griffin, Spencer, & Rogers, 2016; Lorenz & Ziegler, 2009).

In this vein, we here investigate participants with a chronic lesion to the left-hemispheric language network, all of whom showed overt aphasia in the acute stage of their disease and suffered from mild to moderate or residual aphasia at the time of testing. To inquire in how an acquired lesion impacts on lexico-semantic processing, we used a novel semantic interference paradigm as previously investigated in neurotypical young participants (van Scherpenberg et al., 2020). Our results contribute to the question of how semantic context, generated by a set of eight distractor words, affects language production after brain lesions causing aphasic deficits. We used a combined eye tracking and picture naming paradigm, to help provide evidence for two aspects of lexical retrieval: (i) the dynamics of analysis of a set of words regarding their semantic relation and (ii) efficiency and modulation of picture naming in a controlled semantic context. Besides implications for models of language production, the study adds to the growing body of work demonstrating feasibility and fruitfulness of complex language production paradigms in heterogeneous cohorts of people with residual to moderate language impairment.

At the group level, participants showed a strong semantic interference effect elicited by categorically related distractor words. The effect is significantly larger than that in neurotypical speakers. Notably, it is not correlated to clinically applied, linguistic tests including those targeting word-level deficits. In line with findings in the neurotypical cohort, the interference effect is independent of the number of distractor words (i.e., no difference between three, four, and five categorically related distractor words). Also in line with the findings in the neurotypical group, duration of fixation on the semantically related distractor words did not predict naming latency. Although overall naming latencies decreased significantly over the course of the experiment, the interference effect was stable across repetitions of the same picture across all trials. This contrasts findings in the neurotypical group, who showed interference only in the first cycle of naming. Interestingly, eye tracking additionally revealed that participants fixated equally long on all words. Thereby, the preferential fixation of categorically related words in the neurotypical cohort is not preserved in the group of participants with a lesion to the language network. It is noteworthy, however, that participants who showed a preferential fixation on categorically related words performed better in the clinical test assessing overall semantic abilities (NVST). It should be noted that the reported results remained the same when including age as a covariate in the statistical models, showing that the age range of our participants did not influence the group behavior. Instead, the effects are more likely related to the specific changes because of the aphasic deficit and the underling lesion in the language network.

The above behavioral results are complemented by findings of explorative lesion–behavior correlational analyses. Regarding overall semantic abilities, lesions in the ATL correlated with lesser performance in overall semantic (NVST↓) and synonym judgment ($\text{SYNON}^{\text{LEMO}}$↓) abilities. The fact that lesions in similar clusters in the ATL correlate with smaller fixation preference for related compared to unrelated words ($\Delta\text{FIX}^{\text{rel-unrel}}$↓) suggests a common underlying neuronal network. With regard to the semantic interference effect on lexical retrieval, lesions in the posterior MTG and in the STG/planum polare correlate with a smaller interference effects (as evidenced be VOTs: $\Delta\text{VOT}^{\text{rel-unrel}}$↓).

We will first briefly discuss two findings that are in line with the findings in the neurotypical population previously reported (van Scherpenberg et al., 2020). We then discuss the focus of this paper, that is, in how far a brain lesion elicits changes in semantic categorization and overt picture naming, while taking into account the results of our exploratory lesion behavior correlations.

## Naming Latencies Are Independent of the Number of Categorically Related Distractors and the Categorical Fixation Preference

Findings in the clinical and neurotypical group converge in that semantic interference is not affected by set size. For the clinical group, a significant effect is observed at three, four, and five categorically related distractor words (~36, ~38, and ~29 msec, respectively); that is, the effect did not increase with additional distractors. This supports the assumption that reading of more categorically related distractor words does not induce more competition on target word retrieval. Besides number of overtly presented categorical distractors, longer fixation on semantically related distractor words did not increase interference in both PWA and neurotypical groups. This provides confirmatory evidence for the notion that once a threshold is reached, autochthonous, implicit activation of the lexical cohort is triggered leading to competition (Piai, Roelofs, & Schriefers, 2012). The lack of effects of number of categorical distractor words and fixation duration shows that cohort activation does not depend on these two parameters. Lexical competition must be considered a function of pre-established parameters of the specific category, such as size of and semantic proximity within the cohort (Rose, Aristei, Melinger, & Abdel Rahman, 2019; Rabovsky, Schad, & Abdel Rahman, 2016; Aristei & Abdel Rahman, 2013; Vigliocco, Vinson, Damian, & Levelt, 2002).

## PWA Show Large Semantic Interference, Stable across Naming Repetitions

The semantic interference effect observed in PWA is numerically much stronger than that of neurotypical participants (~30 vs. ~10 msec). Moreover, contrary to the neurotypical group, the effect in the clinical population is stable across naming repetitions of the same item. Despite an overall decrease in naming latency across repetitions (~66 msec, on average), the interference effect remained stable (no interaction of picture type and repetition). In the neurotypical group, both overall VOT and the interference effect ($\Delta VOT^{rel\text{-}unrel}$) decreased significantly. This suggests that the lesioned network shows larger vulnerability of the correct lexical retrieval and cannot afford substantial learning of the interference suppression. Alternatively, increasing facilitatory effects within the lexico-semantic network may explain the attenuation of the interference effect as documented in our previously examined neurotypical cohort. The progressive familiarization with the limited number of seven categories would strengthen featural/conceptual aspects of the category. There is converging evidence that, at the conceptual level, facilitation is elicited by semantic membership. Therefore, the larger and persistent interference effect in the present cohort of people with a lesion in the lexico-semantic network may point to a deficit at this level of the naming process. We will come back to this aspect below.

Previous evidence on semantic interference in PWA based on the picture–word–interference task is inconclusive. Some studies demonstrated a robust effect at the group level (Pino et al., 2021; Piai & Knight, 2018; Hashimoto & Thompson, 2010), whereas others failed to report a significant effect in cohorts or in single-case studies (Piai, Riès, & Swick, 2016; Wilshire et al., 2007). Our study adds evidence of the effect in participants with aphasia over and above specific lexico-semantic abilities. The lack of significant correlations to clinical assessments on naming, word fluency, or semantic abilities suggests that standard patholinguistic diagnostics are largely "blind" to interference by categorical distractors. This may be of note for clinical perspectives because categorical distractor-induced interference is qualitatively similar but substantially larger when compared to neurotypical participants.

The explorative VLSM analyses showed lesions in the left lateral-temporal cortex (STG and MTG) to decrease the interference effect. It highlights the region's key role in picture naming, more specifically the suggestion that temporal areas are essential for activation of the lexical target (Baldo, Arévalo, Patterson, & Dronkers, 2013). A decrease in inference may seem counterintuitive at first; however, co-activation of a lexical cohort can be assumed to be likewise affected by the lesion (Harvey & Schnur, 2015; Henseler, Mädebach, Kotz, & Jescheniak, 2014). Interestingly, results of a brain stimulation study in neurotypical participants (Pisoni et al., 2012) have been interpreted in exactly this vein: Less efficient activation of lexical entries reduces the number of co-activated lexical competitors, thereby reducing the inhibitory effect on target retrieval. Our exploratory lesion analysis supports this notion.

## Semantic Interference Does Not Depend on Explicit Acknowledgment of Semantic Category

Neurotypical participants fixated longer on categorically related when compared to unrelated words in the distractor word set. As discussed above, there was no explicit instruction to do so, nor can the preferential fixation on cohort members be considered strategical for the task, which required to name a picture, not contained in the distractor set. The finding in neurotypical participants indicates an acknowledgment or explicit processing of the semantic category present in the word set. Interestingly, this categorization effect was not found in the current study. Participants with aphasia showed no fixation preference for categorically related words. The finding is particularly relevant in that it speaks for a nonstraightforward relationship between categorical semantic processing and lexical retrieval. This requires discussion.

Apart from the picture–word–interference task, blocked cyclic naming and continuous naming paradigms elicit semantic interference and may shed light on the relationship between semantic and lexical processing. In the blocked cyclic naming paradigm, pictures are named consecutively either within homogenous blocks of one semantic category, or heterogeneous blocks of several semantic categories (Crowther & Martin, 2014; Belke & Stielow, 2013; Schnur, Schwartz, Brecher, & Hodgson, 2006; Belke, Meyer, & Damian, 2005). Here, semantic interference reliably appears in the comparison of naming latencies between the two naming settings: Pictures are named more slowly in homogenous than in heterogeneous blocks. By repeated retrieval of members of the same semantic category, their lexical representations form a strong cohort of mutual competitors, constantly inhibiting retrieval of the respective target lexical representation. Recently, it has been debated that the blocked cyclic naming paradigm leaves room for additional, task-related strategies potentially influencing the effect: Because of the repetitively presented semantic categories, neurotypical participants become familiar with the items in the set, which may allow them to bias the lexical-semantic representations of the set members, increasing efficiency of lexical retrieval (Belke, 2017a, 2017b). This suggests that, in the blocked cyclic paradigm, participants are aware of the semantic relationship of the pictures they are naming. Although this effect does not override the inhibition of naming latencies within blocks, it counteracts accumulation of interference across blocks. The assumption is supported by the fact that participants with lesions in the left pFC do exhibit stronger cumulative effects, that is, stronger semantic interference also across blocks (Riès et al., 2015; Belke & Stielow, 2013; Schnur et al., 2009). Lesions in this area, known to be involved in executive control functions and retrieval of semantic knowledge (Thompson-Schill, Bedny, & Goldberg, 2005; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997), may compromise the top–down bias of the lexical-semantic representations of the set members in the respective cycle.

On the contrary, in the continuous naming paradigm (Schnur, 2014; Oppenheim, Dell, & Schwartz, 2010;

Howard et al., 2006), pictures are also named consecutively, but in seemingly random order with category members separated by pictures from other categories as well as fillers. Nevertheless, with each new member of a category that has to be named, latencies have been shown to cumulatively increase (see also Kuhlen & Abdel Rahman, 2017; Rose & Abdel Rahman, 2017). Even though participants are likely not aware of the categorical relationship of the pictures because of their seemingly random distribution, their relatedness nevertheless exerts an inhibitory function on naming latencies. The continuous naming paradigm therefore supports the understanding that explicit processing of a semantic relationship is not necessary to induce interference.

The current study adds to this debate. On the one hand, our study demonstrates robust and large semantic picture–word interference induced by multiple semantic distractors, in a group of participants with chronic lesions in the left-hemispheric language network including the temporal lobe and IFG. However, this effect is not dependent on explicit processing of the semantic category, which participants viewed as part of the circular word set beforehand. Participants fixated equally long on semantically related compared to unrelated words. This pattern is clearly different from our findings in neurotypical participants (van Scherpenberg et al., 2020) but resembles findings in participants with semantic memory impairment. As reported by Seckin et al. (2016) and Faria et al. (2018), individuals with semantic dementia spent more time fixating on unrelated picture foils in a visual world paradigm, compared to neurotypical participants. Participants in this study did not exhibit strong difficulties in semantic processing, as indicated by the clinical tests (LEMO Synonyms; NVST nonverbal semantics tasks; see Table 1). However, correlations between the experimental measures and the test scores revealed that the better participants performed in the NVST, the bigger the difference in fixation durations between category members and nonmembers, indicating a higher ability for semantic differentiation. In addition, the explorative lesion–symptom correlations showed that both lower performance in the NVST and LEMO Synonyms task as well as a decreased difference in fixation durations correlated with lesions in the ATL. The ATL has been described to have the function of a semantic hub integrating multimodal semantic information (e.g., Mesulam et al., 2009, 2013; Pobric et al., 2007). Although interpretation of our VLSM analyses is tentative, results point to an involvement of the ATL in our modified picture–word interference paradigm. We suggest that lexical information from the written words is mapped on their (amodal) semantic correspondence, which would be the prerequisite to explicitly acknowledge their semantic categorical relationship. Lesions in the ATL may compromise this ability, whereas lexical co-activation, as a prerequisite for the interference effect, is largely preserved.

Despite the absence of explicit semantic categorization, naming latencies were significantly delayed when the target picture was categorically related to the distractor word set. Moreover, the effect was even stronger than that in the neurotypical population, who showed a clear semantic categorization effect as evidenced by fixation durations. These findings confirm the assumption that semantic information from lexically activated distractors (be it written distractor words or previously named pictures) is implicitly processed to activate further category members. Although somewhat speculative, the absence of a relationship between frontal (IFG) lesions and either aspect of the experimental task performance may point in the same direction. The implicitly activated category members, in turn, form a cohort of lexical competitors, which inhibit target selection when the target is part of the same semantic category (lexical competition hypothesis, e.g., Abdel Rahman & Melinger, 2009, 2019; Melinger & Abdel Rahman, 2013; La Heij et al., 2006; Wheeldon & Monsell, 1994).

It should be noted that, in our paradigm, the SOA, that is, the time between first presentation of a distractor word and display of the target picture (8 sec), was substantially longer than that in typical picture–word–interference tasks. We used the long SOA to ensure that each word was processed. On average, participants fixated ~720 msec on each word in the word set. Therefore, even if lexicosemantic processing was slowed in our clinical population, the exploration time of 8 sec can be assumed sufficient to retrieve the semantic content of the words and activation of a cohort of competitors. In fact, the single-case study by Wilshire et al. (2007) revealed (a trend toward) semantic interference only after enough time had passed for successful semantic activation of the distractor word (at SOA of +200 or +400 msec). We therefore suggest that the paradigm described here adds further evidence that semantic interference through lexical competition is independent of explicit processing or acknowledgment of semantic information of previously activated distractors of pictures. However, the fact that we do find interference for related compared to unrelated distractor words implies that implicit, automated semantic processing must have taken place for the distractor words to function as competitors inhibiting naming.

## Conclusion

Taken together, the results of the current study add to the knowledge on semantic context effects during word retrieval in aphasia. We applied a complex novel multiword picture–word–interference paradigm combining both naming latency as well as eye movement measures, to examine the relationship between explicit processing of the semantic content of the distractor words and their inhibitory effect on the following naming task. We replicated a robust semantic interference effect from multiple simultaneously presented distractor words, which was substantially larger than that of a neurotypical population in the same paradigm. Comparable to the results from the neurotypical population, the size of the effect did not depend on the number of distractors in the word set and was not modulated by longer fixation durations to the semantically related distractor words. This is in line with the concept that, if activation of a semantic category passes a threshold, the activation of the lexical cohort is implicit and automatic and cannot be augmented by overtly adding members to the lexical cohort or longer processing of the lexical entries does not further modulate lexical competition during the word retrieval process. In the same vein, the interference effect arose despite no explicit processing of the categorical relationship between the distractor words. The participants with a lesion in the lexico-semantic network fixated equally long on members and nonmembers of the semantic category present in the word set. This supports the assumption that implicit, automatic semantic activation upon reading the distractor words is sufficient to cause interference.

Notably, a smaller difference in fixations on category members versus nonmembers correlated with lower nonverbal semantic abilities (in the NVST task) and lesions in the ATL, confirming an involvement of this amodal semantic hub in explicit semantic processing in this task. Because conceptual-level semantics are generally agreed on to facilitate naming, impairment at this level may explain why our clinical cohort showed a larger and persistent interference effect, when compared to the previously tested neurotypical cohort. Future research could corroborate this implication by assessing the relationship of semantic processing and naming abilities in participants with semantic dementia, whose semantic competence is known to be strongly impaired, because of atrophy in the ATL.

## APPENDIX A: STIMULI

**Table A1.** List of Stimuli

| *Category* | *Items* | | | | | |
|---|---|---|---|---|---|---|
| hoofed animals | Reh (deer) | Pferd (horse) | Esel (donkey) | Schaf (sheep) | Kamel (camel) | Ziege (goat) |
| fruits | Apfel (apple) | Birne (pear) | Traube (grape) | Erdbeere (strawberry) | Kirsche (cherry) | Orange (orange) |
| seating furniture | Sofa (couch) | Stuhl (chair) | Hocker (stool) | Sessel (armchair) | Bank (bench) | Thron (throne) |
| carpenter's tools | Hammer (hammer) | Säge (saw) | Schraube (screw) | Axt (axe) | Zange (pliers) | Bohrer (drill) |
| face parts | Auge (eye) | Nase (nose) | Mund (mouth) | Ohr (ear) | Kinn (chin) | Haare (hair) |
| street vehicles | Auto (car) | Lastwagen (truck) | Motorrad (motorcycle) | Kutsche (carriage) | Bus (bus) | Traktor (tractor) |
| upper boddy clothing | Mantel (coat) | Jacke (jacket) | Pullover (sweater) | Hemd (shirt) | T-Shirt (t-shirt) | Bluse (blouse) |

## APPENDIX B: VOT ANALYSES INCLUDING AGE AS COVARIATE

**Table B1.** GLMM Assessing Semantic Interference with Age as Covariate

| | *Response Times* | | | |
|---|---|---|---|---|
| *Predictors* | *Estimates* | *SE* | *Statistic* | *p* |
| Intercept | 1078.39 | 102.88 | 10.48 | < .001 |
| picture type: related vs. unrelated | 34.91 | 15.08 | 2.31 | .021 |
| set size: 4 vs. 3 | −4.89 | 13.59 | −0.36 | .719 |
| set size: 5 vs. 3 | −6.26 | 15.78 | −0.40 | .692 |
| rel vs. unrel × 4 vs. 3 | 15.12 | 27.89 | 0.54 | .588 |
| rel vs. unrel × 5 vs. 3 | 2.41 | 32.39 | 0.07 | .941 |
| age | 5.90 | 1.89 | 3.12 | .002 |

**Table B2.** GLMM Assessing Semantic Interference across Item Repetitions with Age as Covariate

| | *Response Times* | | | |
|---|---|---|---|---|
| *Predictors* | *Estimates* | *SE* | *Statistic* | *p* |
| Intercept | 1138.49 | 7.88 | 144.50 | < .001 |
| picture type: related vs. unrelated | 35.69 | 4.95 | 7.21 | < .001 |
| picture repetition | −61.80 | 3.86 | −16.00 | < .001 |
| picture type × repetition | 4.70 | 5.76 | 0.82 | .414 |
| age | 5.04 | 1.13 | 4.45 | < .001 |

## APPENDIX C: FIXATION DURATIONS

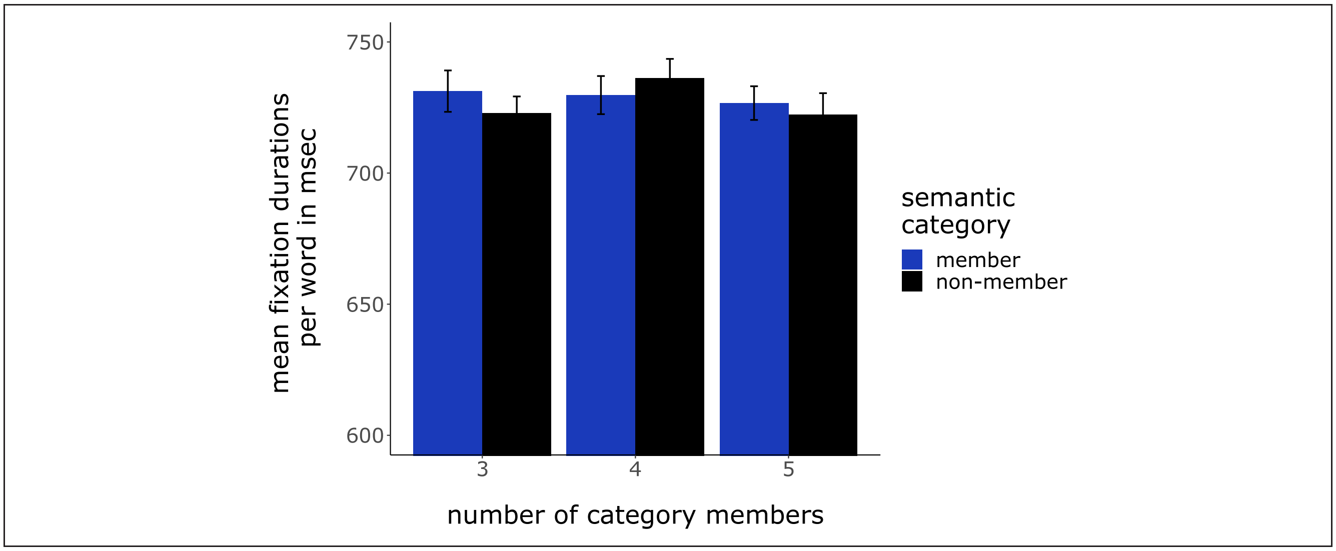

**Figure C1.** Mean fixation durations per word for category members versus nonmembers.

**Table C1.** GLMM Assessing Fixation Durations on Category Members versus Nonmembers with Age as Covariate

| | *Fixation Durations* | | | |
|---|---|---|---|---|
| *Predictors* | *Estimates* | *SE* | *Statistic* | *p* |
| Intercept | 860.22 | 1.51 | 571.44 | < .001 |
| word type: category member vs. nonmember | 2.51 | 1.83 | 1.37 | .169 |
| set size: 4 vs. 3 | 4.44 | 1.03 | 4.29 | < .001 |
| set size: 5 vs. 3 | 0.23 | 1.22 | 0.19 | .850 |
| member vs. nonmember × 4 vs. 3 | −15.05 | 1.08 | −13.96 | < .001 |
| member vs. nonmember × 5 vs. 3 | −1.75 | 3.63 | −0.48 | .631 |
| age | −2.52 | 0.41 | −6.13 | < .001 |

## APPENDIX D: CORRELATIONS WITH CLINICAL LINGUISTIC MEASURES

**Table D1.** Correlations between Experimental Variables and Linguistic Test Scores

| *Linguistic Test Score* | *Experimental Effect* | *Spearman's Rho* | *p Value* |
|---|---|---|---|
| LEMO: Reading | Δ fixation durations | 0.235 | .229 |
| | semantic interference | −0.093 | .637 |
| LEMO: Synonyms | Δ fixation durations | 0.244 | .21 |
| | semantic interference | −0.207 | .29 |
| AAT: Naming | Δ fixation durations | −0.218 | .318 |
| | semantic interference | −0.26 | .231 |
| fluency: animals | Δ fixation durations | −0.12 | .586 |
| | semantic interference | −0.235 | .281 |
| NVST | Δ fixation durations | 0.463 | **.013** |
| | semantic interference | 0.099 | .617 |

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### Diversity in Citation Practices

A retrospective analysis of the citations in every article published in this journal from 2010 to 2020 has revealed a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience (JoCN)* during this period were M(an)/M = .408, W(oman)/M = .335, M/W = .108, and W/W = .149, the comparable proportions for the articles that these authorship teams cited were M/M = .579, W/M = .243, M/W = .102, and W/W = .076 (Fulvio et al., *JoCN*, 33:1, pp. 3–7). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance.

### Notes

1. We use this unspecific term to differentiate from semantic dementia, which is usually subsumed under the primary progressive aphasia umbrella. We do not limit the term "typical aphasia" to the etiology of stroke.
2. Vice versa: If a participant showed a lesion in one single voxel only, the performance deficit could be precisely ascribed to this voxel.

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