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Double dissociation of letter and category fluency following left frontal and temporal lobe lesions

Juliana V. Baldo[a]; Sophie Schwartz[b]; David P. Wilkins[ac]; Nina F. Dronkers[ade]
[a] VA Northern California Health Care System, Martinez, CA, USA [b] University of Geneva, Switzerland [c] University of Sydney, Australia [d] University of California, Davis, CA, USA [e] University of California, San Diego, CA, USA

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Double dissociation of letter and category fluency following left frontal and temporal lobe lesions

Juliana V. Baldo
VA Northern California Health Care System, Martinez, CA, USA

Sophie Schwartz
University of Geneva, Switzerland

David P. Wilkins
VA Northern California Health Care System, Martinez, CA, USA, and University of Sydney, Australia

Nina F. Dronkers
VA Northern California Health Care System, Martinez, CA, University of California, Davis, CA, and University of California, San Diego, CA, USA

Background: A number of studies have suggested that temporal cortex is critical for the ability to generate exemplars belonging to a particular semantic category (i.e., category fluency), while frontal cortex is critical for generating words beginning with a particular letter (i.e., letter or phonemic fluency). However, previous studies have often focused on relative, quantitative differences in performance across groups of patients and primarily in the oral domain.
Aims: The current study analysed verbal fluency data from two individuals with chronic aphasia, one with a large left temporal lobe lesion and a severe Wernicke's aphasia, and a second individual with a large left frontal lobe lesion and a moderately severe non-fluent aphasia. The goal of the study was to do both qualitative and quantitative analyses of letter and category fluency performance in these two individuals across oral and written fluency domains.
Methods & Procedures: Participants were administered both oral and written versions of letter fluency (*FAS*) and category fluency conditions (fruits, animals, and supermarket items). Participants were given 90 seconds to generate as many items as possible, and their responses were scored for both overall output, as well as qualitative structure using a clustering analysis.
Outcomes & Results: The individual with an extensive temporal lobe lesion generated a large number of exemplars on the letter fluency task. Some of these items were neologisms

Address correspondence to: Juliana Baldo PhD, Center for Aphasia and Related Disorders, 150 Muir Rd. (126 R), Martinez, CA 94553, USA. E-mail: juliana@ebire.org

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(e.g., *frest*, *anth*, and *swink*), but remarkably all adhered to the phonological constraints of the task. However, this individual was very poor at generating items belonging to semantic categories. In contrast, the individual with a large frontal lesion generated many exemplars on the category fluency task but only two items on the letter fluency task. The same pattern was replicated in the written domain in both individuals, and results from the clustering analysis paralleled these quantitative findings.
Conclusions: This report describes two individuals with aphasia who exhibited a double dissociation between letter and category fluency performance in both oral and written domains. The current findings provide further evidence for the notion that left frontal cortex is critical for word retrieval based on phonology, while left temporal cortex is critical for word retrieval based on semantics. The findings have implications for the types of strategies that may be most effective in individuals with lesions to these brain regions critical for word retrieval.

Keywords: Wernicke's aphasia; Verbal fluency; Lexical retrieval; Neologism; Jargon aphasia; Temporal cortex; Frontal cortex.

Previous studies have suggested that verbal fluency performance is mediated by distinct brain regions, depending on the type of word retrieval involved. Category fluency tasks that require participants to retrieve exemplars of a particular semantic category (e.g., animals) have been associated with left temporal cortex, whereas letter or phonemic fluency tasks, in which participants retrieve words based on a given letter (e.g., words beginning with *F*), have been associated with left frontal cortex. These findings come from a variety of sources, including functional neuroimaging (Gourovitch et al., 2000; Mummery, Patterson, Hodges, & Wise, 1996) and studies with brain-injured individuals (Baldo, Schwartz, Wilkins, & Dronkers, 2006; Butters, Granholm, Salmon, Grant, & Wolfe, 1987; Janowsky, Shimamura, Kritchevsky, & Squire, 1989; Miller, 1984; Milner, 1964; Monsch et al., 1994; Perret, 1974; Stuss et al., 1998; Villki & Holst, 1994). Generally, these latter studies with brain-injured individuals have shown that patients with focal frontal lesions are relatively impaired at letter fluency tasks, while patients with temporal lobe dysfunction show a disproportionate deficit on semantic fluency. In some reports, however, frontal dysfunction has been reported to disrupt both letter and semantic fluency, presumably due to the demands that both tasks place on cognitive control mechanisms, such as self-monitoring, initiation, and strategic retrieval (see meta-analysis by Henry & Crawford, 2004). In a recent study using voxel-based lesion symptom mapping (VLSM), Baldo et al. (2006) found that lesions in left frontal cortex were more strongly associated with letter fluency and lesions in left temporal cortex were more associated with category fluency. Similarly, functional-imaging studies have shown relatively greater activation in left frontal regions during letter fluency tasks and greater activation in left temporal cortex during category fluency tasks (Gourovitch et al., 2000; Mummery et al., 1996). This dissociation has also been studied using dual-task paradigms in which normal participants execute a concurrent task while generating items for the letter or category fluency condition. Such studies have found that a concurrent task that is putatively dependent on frontal cortex (e.g., finger tapping) is more disruptive to letter fluency, while a concurrent task more dependent on temporal cortex (e.g., object decision) is more disruptive to category fluency performance (Martin, Wiggs, Lalonde, & Mack, 1994; Moscovitch, 1994).

While this dissociation between letter and category fluency has been supported by a variety of methodologies, the studies have been based primarily on quantitative

comparisons of relative performance across conditions (e.g., individuals with temporal lobe lesions generate relatively fewer items on semantic versus letter fluency) and most often only in the oral domain. Also, fluency performance is rarely purely letter based or purely semantic without some cross-contamination; for example, evidence of semantic clustering is readily apparent when participants are generating words starting with a given letter (e.g., *ant ... aardvark*; Schwartz, Baldo, Graves, & Brugger, 2003). In the current study, we had the opportunity to study two individuals in depth who had extensive lesions that effectively left each of them with an isolated ability to generate primarily letter-based or semantic-based responses without cross-contamination. Despite their dense aphasia, we were able to elicit fluency responses from these two individuals and observed profound deficits in letter fluency in one and category fluency in the other across both oral and written domains. Moreover, analysis of the *quality* of their responses provided insights into the mechanisms underlying these two types of word retrieval.

METHOD

Participants

Two individuals with chronic aphasia participated in the study. The first was a 75-year-old man who was 23 months post-stroke at the time of testing. He suffered a single left hemisphere stroke due to a middle cerebral artery occlusion. A recent MRI showed that his lesion encompassed a large portion of the middle and superior temporal gyri, as well as a small portion of inferior parietal cortex (see Figure 1). The lesion involved both the cortex as well as the underlying white matter. We will refer to him as TL (for temporal lobe stroke). His pre-morbid medical history was unremarkable with respect to neurological and psychiatric events. He was a right-handed, native English speaker with 16 years of education. At the time of testing, he presented with circumlocutory, fluent speech characterised by a mixture of paraphasias, neologisms, and real words. He classified as having Wernicke's aphasia on the Western Aphasia Battery (WAB; Kertesz, 1982). Details of his language and cognitive testing are provided in Table 1.

The second individual was a 54-year-old woman who was 8 years post-stroke when tested. She suffered a middle cerebral artery stroke that resulted in a large left frontal lesion that also impinged on a small portion of anterior temporal cortex and the basal ganglia (see Figure 1). We will refer to her as FL (for frontal lobe stroke). She had no prior neurological or psychiatric history. She was a native English speaker and had 20 years of education. On an assessment of pre-morbid handedness, she reported being right-handed for most activities (19/20), but said she could also do some of the activities with her left hand (10/20, not including writing). She presented with dysfluent speech that was at times telegraphic, consistent with her frontal lesion. On the WAB, she classified as having conduction aphasia, although her clinical presentation was more that of mild Broca's aphasia. Her large fronto-insular lesion was also more consistent with this clinical impression (see Table 1 for details of language and cognitive testing).

The participants, as well as their caregivers, read and signed consent forms prior to testing. Testing was approved by the Institutional Review Board of the VA Northern California Health Care System, Martinez, CA and was in keeping with the Helsinki Declaration.

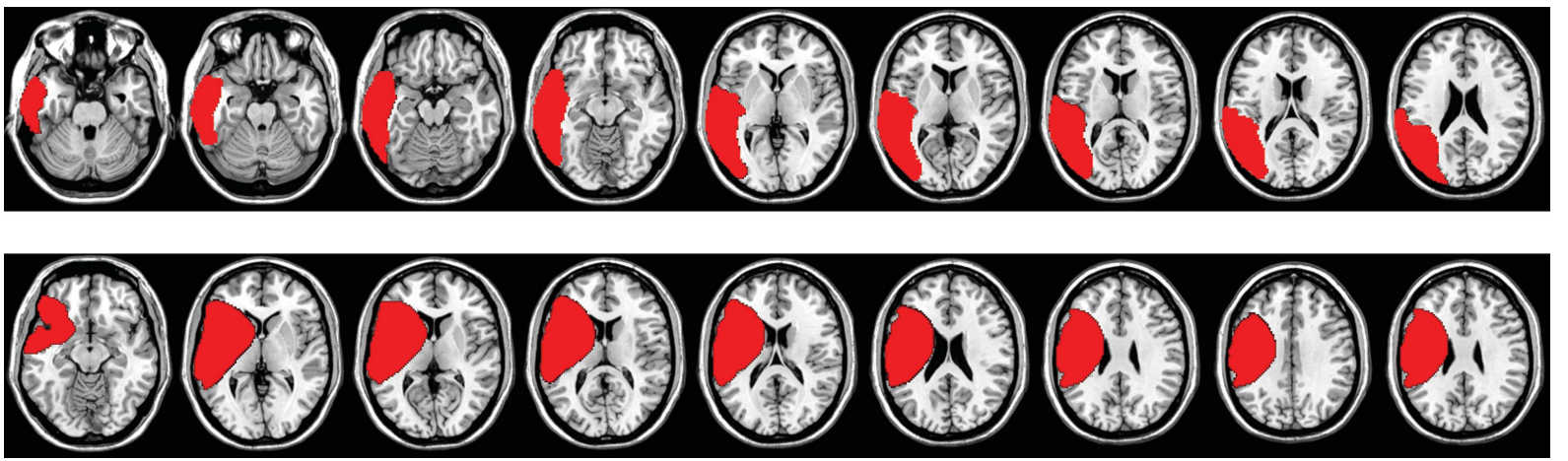

Figure 1. Top panel shows lesion reconstruction of participant TL's large temporal lobe lesion (shown in red online; and in dark grey in print) that involved the middle and superior temporal gyri and a small segment of inferior parietal cortex. Bottom panel shows FL's large frontal lobe lesion that involved inferior and middle frontal gyri, as well as a small portion of anterior temporal cortex. [To view this figure in colour please visit the online version of this Journal.]

TABLE 1
Language and cognitive testing results

	TL	*FL*
Speech fluency	80%	50%
Repetition	20%	50%
Comprehension	40%	80%
Naming	30%	80%
Reading/Writing	65%	55%
AQ	48.7	66.7
Block Design	89%	56%
Calculation	92%	58%
Drawing	90%	58%
Raven's CPM	62%	46%
CQ	47.5	67.8

Scores transformed into percentage of total points possible on each subtest. AQ = aphasia quotient, which is an overall score out of 100 on the WAB. Raven's CPM = Raven's Coloured Progressive Matrices. CQ = cognitive quotient, which is an overall score out of 100 on the WAB that incorporates both language and cognitive test performance.

Materials and procedures

Letter and category fluency tasks were administered to the participants as part of a larger neuropsychological battery that included both language and cognitive testing. In the letter fluency task, participants were first asked to name words beginning with the letter *F*. (TL was unable to understand these instructions, so the examiner wrote out the letter *F* with a line after it and gestured for him to speak.) The examiner recorded the participants' responses for 90 seconds (longer than the standard 60 seconds), in order to observe how the quality and quantity of the individuals' responses changed over a longer interval (see Ober, Dronkers, Friedland, Koss, & Delis, 1986). The participants were subsequently asked to generate words beginning with the letters *A* and then *S*. Following letter fluency, they were given 90 seconds to generate items belonging to the semantic categories *fruits*, *animals*, and *things you can buy at a supermarket*, in that order. TL perseverated on generating items beginning with the same letter during category fluency. Thus he was re-tested on all conditions in a second session 3 weeks later, with the category fluency task administered first.

In a separate session, both individuals' fluency performance was tested in the written domain by instructing them to write words beginning with the different letter cues (*F*, *A*, and *S*) and words belonging to semantic categories (*fruits*, *animals*, and *supermarket*) for 90 seconds each. Similar cueing as described above was used for both individuals, but here the examiner wrote the letter cue (e.g., *F*) or category cue (e.g., *fruits*) at the top of each page. We included this written fluency condition to insure that the results were due to core language deficits, rather than other deficits that can affect speech output/language production (e.g., dysarthria, apraxia of speech).

Fluency responses were scored as valid words, repetitions, or neologisms. Here we use the term *neologism* to refer to both simple and complex paraphasic errors (i.e., any item that was not recognisable as an English word). We did not attempt to distinguish between paraphasic errors and neologisms (which can be thought of on a

continuum from simple to complex phonemic errors), because it was not possible to be sure of the target word.

RESULTS

The two individuals with aphasia, TL with a large temporal lesion and FL with a large frontal lesion, showed opposite patterns of performance on the letter and category fluency tasks (see Tables 2–4). TL generated a large number of items in the oral letter fluency task (*FAS*), 51 in Session 1 and 85 in Session 2. Samples of his responses from a single session are provided in Table 3. Interestingly, although many of his responses were neologisms, the items still adhered to the letter constraints of the individual conditions and generally met the phonological and phonotactic constraints of English. In the first testing session, he insisted on spelling his responses during the letter fluency task, including his neologisms (e.g., *a-l-l, all, a-s-t, ast, a-n-t, ant, a-l-l-o-w, allow, a-w-a-r-k, awark*, etc.). This spelling behaviour likely prevented him from producing even more items within the time limit. Remarkably, the spellings that he provided were correct in the case of the real words and reasonable English spellings for the neologisms. In contrast, he generated far fewer valid items on the category fluency task. For example, he generated just nine items in the *Fruits* condition, and only two of those were appropriate and novel responses (*apples* and *oranges*).

Similar to his performance in the oral domain, TL exhibited relatively good performance for letter fluency in the written domain. For example, in the *F* condition, he wrote 20 items in 90 seconds, all of which started with *F* and only six of which were unacceptable responses (i.e., repetitions and neologisms; see Figure 2). In contrast, on the written *Fruits* condition, this individual wrote just six items, only one of which was appropriate (*apple*).

In contrast, the individual with the left frontal lesion (FL) showed the reverse pattern of performance on the fluency tasks (see Tables 2 and 4). In both the oral and written

TABLE 2
Verbal fluency performance

	TL	*FL*
Oral letter fluency performance (total of FAS)		
Neologisms	18*	0
Repetitions	10*	0
Valid words	34.5*	2
Oral category fluency performance (total of three categories)		
Neologisms	5	0
Repetitions	9	0
Valid words	6	35
Written letter fluency performance (total of FAS)		
Neologisms	27	0
Repetitions	9	0
Valid words	21	5
Written category fluency performance (total of three categories)		
Neologisms	9	0
Repetitions	2	0
Valid words	6	22

*Averaged across sessions 1 and 2.

TABLE 3
Oral fluency responses produced in 90 s by the individual with a large temporal lobe lesion

F	*A*	*S*	*Fruits*	*Animals*	*Supermarket*
free	*all*	*sew*	*apples*	*dogs*	*book*
fun	*ump*	*seat*	*apples*	*cats*	*/univent/*
from	*about*	*sear*	*books*	*books*	*book*
free	*/awin/*	*sound*	*green*	*elephant*	*apples*
/frest/	*apple*	*sink*	*yellow*	*bank*	*books*
fat	*all*	*strip*	*apple*	*/silingen/*	*free books*
fall	*/anth/*	*sink*	*apples*	*single*	*books*
frank	*ants*	*sin*	*oranges*	*single book*	*cable*
free	*ant*	*sand*	*yellow*	*apple*	*table*
eat	*/ack/*	*/somother/*		*books*	*book*
fat	*apple*	*sound*		*breaks*	*think*
free	*announce*	*sink*		*pants*	*book*
fun	*apple*	*sat*		*yellows*	*tank*
from	*/approse/*	*seep*			*jealous*
fall	*/akint/*	*sort*			*Fremont*
	account	*sink*			*truck*
	endeavor	*sleeve*			*Campbell*
	allow	*sup*			
	acre	*spout*			
	akin	*sand*			
	ants	*/sagillate/*			
	auntie	*sandy*			
	a mother	*/solt/*			
	a dolly	*/sopen/*			
	a girl	*/sapen/*			
	announce	*sink*			
	a love	*/stro/*			
	allowed	*/sart/*			
		/swith/			
		/swink/			
		/sunbet/			
		/sunbes/			

For the letter category "A" we transcribed a number of items with the article "a" preceding the word because the subsequent word could stand on its own (e.g., "a dolly"); however it was not possible to be certain what this individual intended, due to the severe Wernicke's aphasia. These items were not counted as correct responses.

domains, she was able to generate exemplars belonging to a specific semantic category but had difficulty when trying to generate items starting with a given letter. For example, in the oral domain, she provided 17 supermarket items but could not provide a single word starting with the letter *A* and only gave a single response for the cues *F* (*flower*) and *S* (*saw*). Moreover, her category fluency performance showed evidence of semantic clustering (*fruit, celery, peas, corn, chicken, beef, chops ...*), suggesting preserved structure of lexical-semantic knowledge (see below for further analysis).

A similar pattern was also observed for FL in the written fluency conditions. She generated 22 valid items belonging to semantic categories in the written domain but only 5 words beginning with *F*, *A*, and *S*. However, she misspelled many of her responses in the written fluency conditions (e.g., she said "apple", as she spelled *appeal*). This spelling deficit also contrasts with TL's behaviour. TL exhibited a surprisingly good facility for English spelling rules, even as applied to neologisms.

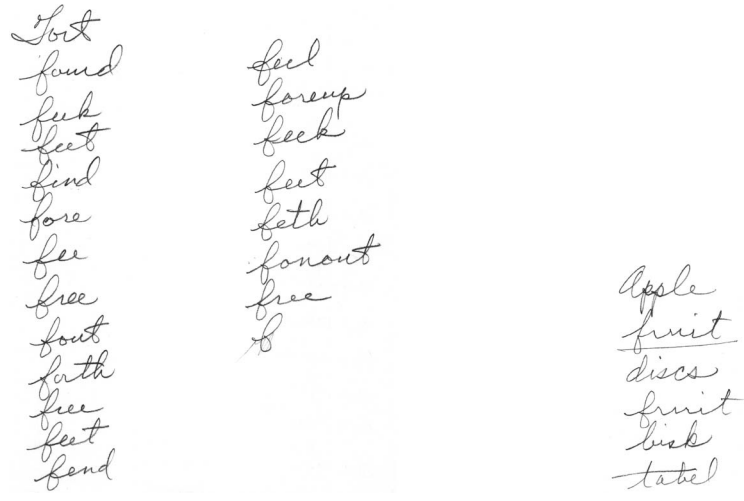

Figure 2. Sample performance in the individual with a large temporal lobe lesion on written letter fluency (F, left) and category fluency (fruits, right).

Last, given the interesting pattern of data, we did a more qualitative analysis of the participants' responses, based on norms for clustering provided by Troyer (2000). The participants' cluster scores were calculated and compared to the Troyer norms for the oral letter fluency task (*FAS*) and for the oral category fluency task (*Animals+ Supermarket* items only, as there were no norms for the *Fruits* condition). For TL, cluster scores were based on responses from the second session. Based on Troyer, clustering on the letter fluency task refers to phonemic clustering, as defined by successively generated words that either (1) begin with the same first two letters, (2) rhyme, (3) have the same first and last sounds, or (4) are homonyms. Clustering on

TABLE 4
Oral fluency responses produced in 90 s by the individual with a frontal lobe lesion

F	*A*	*S*	*Fruits*	*Animals*	*Supermarket*
flower		*saw*	*apple*	*dog*	*t.p.*
			oranges	*cat*	*fruit*
			banana	*bird*	*celery*
			pears	*giraffe*	*peas*
			kiwi fruits	*chimpanzee*	*corn*
			cantaloupe	*rabbit*	*chicken*
			watermelon	*elephant*	*beef*
				giraffe	*chops*
				/teetah/	*seven-up*
				whales	*coke*
				snake	*potato chips*
					coffee
					tea
					cocoa
					milk
					butter
					cheese

the category fluency task refers to semantic clustering, which is defined as successively generated words that belong to the same subcategories (e.g., African animals, water animals, pets, reptiles, etc.). As per Troyer, repetitions and intrusions were included in the cluster score calculation, and thus we included TL's neologisms in the calculations.

Paralleling the quantitative data above, TL had a normal cluster score for letter fluency (43rd percentile) but an impaired cluster score for category fluency (1st percentile). In contrast, FL exhibited a normal cluster score for category fluency (42nd percentile) and an impaired cluster score for letter fluency (2nd percentile). It should be noted that the two impaired cluster scores were necessarily based on the very few responses provided in those conditions; however, the main motivation was to confirm that successful verbal fluency (letter fluency in TL, category fluency in FL) reflected intact underlying phonological and lexical-semantic networks, respectively.

DISCUSSION

The current findings demonstrate a striking double dissociation between letter-based and semantic-based word retrieval in two individuals with severe and chronic aphasia, one with a large left temporal lobe lesion and one with a large left frontal lobe lesion. The individual with the temporal lobe lesion had Wernicke's aphasia but nonetheless was able to generate items on a letter fluency task that obeyed the phonologic constraints of the task. Some of the items were neologisms that began with the appropriate cued letter and conformed to conventional English word form and phonology. He even spontaneously provided reasonable spellings for some of the items, including the neologisms. This preserved ability was also observed in the written domain, as he was able to write a large number of items (including some neologisms) that began with the correct letter. However, he was very poor at generating items belonging to simple categories such as fruits and animals. In contrast, the individual with the frontal lobe lesion showed the reverse pattern: She could generate items belonging to semantic categories but had great difficulty generating words starting with a given letter. This reversed pattern of fluency performance was observed in both the oral and written domains.

In addition to the quantitative findings, we used a more qualitative approach developed by Troyer, Moscovitch, Winocur, Alexander, and Stuss (1998) to calculate the degree to which individuals exhibit phonemic and semantic clustering in verbal fluency data (see also Troyer, 2000). This analysis revealed a similar pattern of dissociation; namely, the individual with the temporal lobe lesion exhibited impaired semantic clustering with preserved phonemic clustering, while the individual with the frontal lobe lesion exhibited impaired phonemic clustering with preserved semantic clustering. These data are in keeping with previous group studies of verbal fluency (e.g., Baldo et al., 2006; Gourovitch et al., 2000; Milner, 1964; Monsch et al., 1994) and further reinforce the notion that the left temporal lobe supports retrieval based on lexical-semantics while the left frontal lobe supports retrieval based on phonological cues.

A number of studies have shown that individuals with temporal lobe dysfunction (e.g., Alzheimer's disease) are relatively poor at generating items belonging to a semantic category (Butters et al., 1987; Davis et al., 2010; Monsch et al., 1994). This deficit has been attributed to the breakdown of semantic-conceptual knowledge, which is presumably disrupted by temporal lobe disease (Chan et al., 1993; Rohrer, Wixted, Salmon, & Butters, 1995). It has also been proposed that this deficit might

be due to a failure to retrieve lexical information (see Ober, 1999), perhaps specifically a deficit in retrieving nouns (Davis et al., 2010). The current study suggests that a similar pattern of deficits may occur in individuals with Wernicke's aphasia (and large temporal lobe lesions) whereby conceptual networks are disconnected from their corresponding lexical or phonological labels.

One could presume that the individual with the temporal lobe lesion (TL) in the current study may simply have a more general semantic deficit leading to reduced category fluency (e.g., Wayland & Taplin, 1982). However, in other neuropsychological testing, this individual was 100% correct on an experimental triadic comparison task in which he had to pair drawings based on their semantic content in task (e.g., a crown with a castle) and was also 100% accurate at sorting colour photos into groups of separate categories (e.g., tools, clothes, etc.) without cueing. Thus this individual appeared to have intact knowledge about semantic categories but a severe deficit in generating labels for those items, typical of many individuals with Wernicke's aphasia (Bose & Buchanan, 2007). We have since observed another individual with severe Wernicke's aphasia who showed a similar ability to generate items (mostly neologistic) on the letter fluency task along with an inability to generate category fluency items.

The individual with the temporal lobe lesion showed surprisingly preserved spelling ability despite his severe Wernicke's aphasia, suggesting that when he generated words (and neologisms) in the letter fluency task, he likely engaged phonologic processes (mediated by frontal cortex) without activating lexical-semantic nodes in the temporal lobe (Rohrer, Rossor, & Warren, 2009). This notion is consistent with previous findings in individuals with jargon aphasia, which suggest that neologisms are the result of a *random phoneme generator* that randomly selects and strings phonemes together *in a phonotactically regular manner* (Butterworth, 1979, p. 152; see also Hanlon & Edmondson, 1996; and see Marshall, 2006, for a review).

In an attempt to understand his production, we asked TL to explain some of the items he had generated in the written letter fluency task. When asked the meaning of the item he had written, *agolf*, he responded with "my golf..golf." This individual was an avid golfer. When asked about the item *funout*, he responded by saying "funout f-u-n-o-u-t ... find out." However, for a number of other items TL seemed perplexed when he read his words aloud and attempted to explain them. Thus in some instances the items appeared to be literal paraphasias of words that he intended, while in other cases the items appeared to be more the result of random phoneme/syllable generation, unconstrained by lexical-semantics. However, making this distinction, especially in the absence of a known target, is very difficult (Stenneken, Hoffman, & Jacobs, 2008).

While TL was impaired on retrieval based on semantic categories, the individual with the frontal lobe lesion (FL) was impaired on word retrieval based on letter cues, generating only two items across three letter categories for 90 seconds each. Her performance is consistent with a number of neuroimaging and lesion studies of letter fluency, showing a relatively greater role of anterior brain regions in letter-based word retrieval. However, the underlying cognitive processes involved are less clear (Schwartz & Baldo, 2001). Some studies have linked regions of lateral frontal cortex to the construction of word forms (Burton, 2001), phonemic processing (e.g., Siok, Jin, Fletcher, & Tan, 2003), or phoneme to grapheme conversion (e.g., Omura, Tsukamoto, Kotani, Ohgami, & Yoshikawa, 2004). Such characterisations are consistent with this individual's poor spelling ability on the written fluency tasks.

At the same time, FL performed relatively well when retrieving items from semantic categories. Based on her overall language performance (80% correct on both comprehension and naming), FL was clearly able to maintain and interpret phonological information for comprehension and able to retrieve lexical phonological forms for confrontation naming. Therefore, the difficulty for FL appeared to reside in her inability to initiate a search based on phonological cues. This case helps elucidate the debate as to whether left frontal cortex is critical for both letter and category fluency (due to its role in strategic, executive processes) or whether it is critical primarily for letter fluency. The case of FL suggests that the latter may be true, as category fluency can be shown to be intact in the face of greatly disrupted letter fluency following a left frontal lesion.

In conclusion, the current study describes two individuals with chronic aphasia who showed a double dissociation in letter and category fluency performance across both oral and written domains. Specifically, an individual with Wernicke's aphasia and a large left temporal lesion was impaired at category fluency but relatively good at letter fluency, while another individual with a large frontal lesion showed the opposite pattern. Unlike previous studies showing relative dissociations between groups of participants, these findings provide a more clear-cut picture of how the left temporal lobe and left frontal lobe function in isolation to support word retrieval. These observations corroborate and extend previous studies of verbal fluency by demonstrating that left frontal cortex is critical for word retrieval based on phonology but not semantics while temporal cortex is critical for word retrieval based on semantics but not phonology. Our findings have potential implications for clinical treatment, as individuals with large temporal lobe lesions/Wernicke's aphasia would benefit from treatments emphasising the link between semantics and the lexicon, while individuals with frontal injury may benefit from treatments emphasising phonology.

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